Comparison of hematological parameters, iron levels, and oxidative stress in women with and without breast cancer: A case-control study

Afsaneh Rajizadeh, Hassan Mozaffari-Khosravi, Javad Zavar-reza, Seyyed Mostafa Shiryazdi

Received: 23 Dec 2016 Published: 20 Dec 2017

Abstract

Background: Iron is one of the nutrients that has recently received considerable attention because of its dual role in the incidence of breast cancer. The present study aimed at comparing hematological parameters, iron levels, and oxidative stress in women with and without breast cancer.

Methods: The participants in this case-control study were 55 women, of whom 26 were new cases of breast cancer (confirmed by biopsy) as the case, and 29 without cancer (confirmed by mammography) as the control group. All participants underwent blood testing for complete blood count (CBC (free iron, ferritin, total iron binding capacity) TIBC (2, 2-diphenyl-1-picrylhydrazyl (DPPH), and Malondialdehyde (MDA)).

Results: The mean±SD age of the participants was 44.25±9.82 years, and there was no significant difference between groups. Also, no statistically significant difference was found between the 2 groups in variables, except the mean corpuscular volume of red cells (MCV), mean corpuscular hemoglobin concentration (MCHC), and mean cell hemoglobin (MCH). The use of iron supplements was significantly higher in the control than in the case group (p=0.01), with an odds ratio of 0.19% (95% CI: 0.45-0.7). The mean serum DPPH was significantly higher in the control than in the case group (p=0.006), but comparison of serum MDA showed no significant difference between the 2 groups.

Conclusion: Iron deficiency anemia was greater in patients with breast cancer than in those without it. Moreover, iron supplementation appears to have a protective effect against breast cancer incidence. In addition, serum DPPH, as a total antioxidant index, was significantly higher in the control group.

Keywords: Iron status, Breast cancer, Oxidative stress, Premenopausal

Introduction

Breast cancer is the most common form of cancer in women worldwide; 1.1 million new cases of breast cancer are diagnosed annually (1); its prevalence is estimated to be 10% in the United States, 8% in Europe, and 1% in Asia (2); its frequency is significant in Iran at 22 per 1000 population. A serious concern in Iran is that the average age of developing the disease is 10 years earlier than in other countries (3).

Breast cancer is a progressive malignant disease of breast tissue (4), and its warning signs are changes in the appearance of the breast including asymmetrical breasts, liquid excretion from the nipple, skin decompensation, and a palpable mass in the breast (5). The disease recurs in 30% of cases, leading to metastasis and malignant forms of cancer (6). It is estimated that annually 458 000 million people lose their lives to this disease worldwide (7). As breast cancer is one of the most expensive cancers to treat (3), its treatment imposes heavy costs on patients and the government (8). Breast cancer is a multifactorial disease (9). Studies show that the presence of genetic and heredi-
Body iron status, oxidative stress, and breast cancer
dary mutations in breast genes BRCA1/BRCA2 is found in
only 5% to 10% of cases (5). Environmental factors, such as
age, infertility, age at first pregnancy, age at meno-
pause, and use of hormones (estrogen or progesterone)
after menopause, play greater roles in development of the
disease (9). Although estrogen has a better-known role in
the pathogenesis of breast cancer (10), the effect of nutri-
tion on the incidence of the disease has also been consid-
ered in recent years (11).
Research has shown that diet affects tumor growth by
altering the metabolism of cancer cells in the latency peri-
od (12). Various studies have assessed the effect of mi-
cronutrients and minerals on the incidence of and im-
provements in breast cancer (13-15), among which the
role of iron in the pathogenesis of breast cancer is still
controversial (16).
Iron is a trace element that plays a vital role in the hu-
man body (17). The most important function of this ele-
ment is in the structure of hemoglobin as a carrier of oxy-
gen in the blood (18). In addition, iron acts as a coenzyme
to many enzymes and is a structural component of myo-
globin (19). Regulation of iron homeostasis in the body is
crucial. Iron also acts like a double-edged sword (20): the
lack of iron causes iron deficiency anemia, which limits
the delivery of oxygen to tissues, and its accumulation
causes iron overload, increases oxidative stress, and pro-
duces free radicals in the body (21). This also points to a
dual role for iron in breast cancer (16).
Because iron overload and iron deficiency are both
problematic states (16), it is important to balance this ele-
ment in the body (21). The prevalence of anemia in Iran is
20% to 30% (22), but a number of foods enriched with
this element are available (23). This poses the dilemma
of whether iron deficiency plays a more important role in
the pathogenesis of breast cancer than its overload.
Considering the increased incidence of this cancer in Iran
and the need for its prevention (24), the present study aimed at
comparing hematologic parameters, iron status, and oxida-
tive stress in women with and without breast cancer.

Methods
Study design and participants
This case-control analytic study was conducted from
May 2014 to May 2015. The volunteer participants were
26 women diagnosed with breast cancer and 29 women,
who were confirmed to be free of breast cancer. Inclusion
criteria for the case group were as follow: females aged 25
to 65 years, a positive breast tissue biopsy, receiving no
interventional treatment, no history of cysts or other cans-
cers, no history of hormone replacement therapy (HRT),
and no history of cardiovascular or hepatic disease, diabe-
tes, or thalassemia. Inclusion criteria for the control group
were as same as the case group, but without incidence of
breast cancer, as confirmed by mammography. Individuals
in both groups were frequency-matched by age and the
presence or absence of menopause.
At the beginning of the project, this study was approved
in the Health College’s Research Council of Shahid
Sadoughi University of Medical Sciences; then, 4 hospi-
tals in the city of Yazd in Iran (Shahid Sadoughi, Gou-
darz, Shahid Rahnemoon, and Seyyed al-Shuhada) were
coordinated for sampling. After informed consent was
obtained from all participants, blood samples were taken
from patients meeting the inclusion criteria with suspected
breast cancer before surgical biopsy of breast tissue after
they gave consent to participate in the study. The patholo-
gy was examined by a physician at 15 days post-biopsy,
and the patients with a confirmed diagnosis of breast can-
cer were included in the case group. The controls were
selected from those patients who referred to the mammog-
raphy section of the same hospital and whose mammogra-
phy results confirmed no signs of cancer, as assessed by
the physician. The patients who met the inclusion criteria
were called and invited to provide a blood sample at the
laboratory, if they were willing to participate.

Measurements
Five mL of fasting venous blood was collected from all
participants to measure biochemical parameters. Blood
sample was taken at between 7 to 8 AM. Serum samples
were produced from blood samples by centrifugation
(1500 to 2000 g) for 10 minutes and were frozen in micro-
tubes at -70°C. After receiving the pathology results, the
samples were tested, while preserving the requirements.
All tests were performed at Shahid Sadoughi hospital la-
boratory.
Each participant completed a 24-hour dietary recall
questionnaire and provided demographic information. For
anthropometric assessment, weight was measured using a
Seka digital scale (Germany), with an accuracy of ±100 g
and minimum coverage. The tests performed were CBC,
TIBC, ferritin, free iron, total protein, and oxidative stress
indices, Malondialdehyde (MDA), and serum 2, 2-
diphenyl-1-picrylhydrazyl (DPPH). CBC was measured
using the Sysmex KX-21® automated hematology analyzer
(Sysmex, Wakinohama kaigandori, Japan), and serum
free iron was measured by the photometric method using
the Ferrere kit (Biorexfaris, Shiraz, Iran). The normal
range of serum-free iron for females, according to manu-
facturer instructions (by age), was 37-149 μg/dL. TIBC
was measured by direct method using a kit (ZiestChem-
Diagnostics, Tehran, Iran), for which the normal range in
females was 250-450 μg/dL (by age). Serum total protein
was measured by the photometric method using a total
protein kit (Pars Azemun, Tehran, Iran), for which the normal range in
females was 6.6-8.8 g/dL. Serum ferritin was measured by direct method using a kit (Accu-
-lite Clia Microwells Ferritin Test System, California,
USA), for which the normal range for females was 10-126
ng/mL (by age).
DPPH and serum MDA were tested by biochemistry
experts in the laboratory in the following manner: The
total antioxidant capacity of total plasma TAC, measured
by the resuscitation combination of DPPH-1, 1. The 20 μL
of plasma was added to phosphate buffer at pH= 7.4 and
then incubated in a methanol solution of DPPH for 30
minutes. The absorbance volume was then read at 517 nm,
and the trapped capacity of DPPH was calculated as
DPPH= (A-AX)/A × 100, in which A denotes DPPH ab-
sorption with methanol, and AX denotes DPPH absorbed
with plasma. The TAC measurement was reported based on the percentage of reduction of plasma DPPH (25).

MDA was measured by thiobarbituric acid reaction (TBARs) using the Calorimetry method. Briefly, 0.5 mL of plasma or standard 3 mL phosphoric acid with 1 mL aqueous 0.6% Barbituric acid (TBA) was placed in a water bath for 45 minutes. After cooling, 4 mL of n-butanol was added and mixed. The n-butanol phase was separated by centrifugation, and the light absorbance in 523 nm was read with a spectrophotometer and reported using the MDA standard based on nmol/mL plasma (26).

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration, and its later amendments or comparable ethical standards.

Statistical analysis

SPSS 16 software was used for data analysis. Student t test was used to compare the means. To compare the frequency distributions of qualitative variables, chi square test was used. A p-value less than 0.05 was considered significant. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were computed. Moreover, N4 software was used to analyze the nutritional data. After data analysis, the participants were divided into 3 groups based on iron measurement indicators: (1) those with normal levels of iron (hemoglobin of 12-16 g/dL and ferritin levels below 150 μg/l), (2) those exhibiting iron deficiency anemia (ferritin below 10 μg/l and hemoglobin below 12 g/dL), (3) and those exhibiting iron overload (ferritin above 150 μg/dL) (28). The values were considered significant at p< 0.05.

Results

Of the 55 participants, 26 (47.3%) were in the case and 29 (52.7%) in the control groups. All participants were married, with a mean±SD age of 44.25±9.82 years (45.92±11.33 years in the case group and 42.75±8.15 years in the control group), but the difference was not statistically significant (p= 0.10). Table 1 demonstrates that mean dietary intake and body weight were not significantly different between the groups; however, mean iron level was higher in the case group than the control group.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case group (n=26)</th>
<th>Control group (n=29)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>2445.91±575.09</td>
<td>2375.29±525.62</td>
<td>0.65</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>80.86±18.07</td>
<td>76.42±27.74</td>
<td>0.51</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>360.69±89.50</td>
<td>343.50±77.81</td>
<td>0.47</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>78.65±25.58</td>
<td>77.94±21.85</td>
<td>0.91</td>
</tr>
<tr>
<td>Iron(mg)</td>
<td>21.47±9.94</td>
<td>24.49±8.78</td>
<td>0.25</td>
</tr>
<tr>
<td>Vitamin D(µg)</td>
<td>2.16±3.62</td>
<td>1.20±1.38</td>
<td>0.20</td>
</tr>
<tr>
<td>Vitamin E(mg)</td>
<td>2.62±2.58</td>
<td>3.10±2.74</td>
<td>0.52</td>
</tr>
<tr>
<td>Vitamin A(RE)**</td>
<td>702.42±387.57</td>
<td>723.91±366.27</td>
<td>0.84</td>
</tr>
<tr>
<td>Weight(kg)</td>
<td>66.75±8.54</td>
<td>65.05±5.29</td>
<td>0.46</td>
</tr>
<tr>
<td>Gravida</td>
<td>4.05±2.66</td>
<td>3.23±1.63</td>
<td>0.21</td>
</tr>
<tr>
<td>Number of breastfeeding</td>
<td>3.29±2.25</td>
<td>2.73±1.51</td>
<td>0.33</td>
</tr>
<tr>
<td>The last lactation (years ago)</td>
<td>13.11±10.12</td>
<td>14.57±9.48</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case group (n=26)</th>
<th>Control group (n=29)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>4.70±0.70</td>
<td>4.57±0.41</td>
<td>0.27</td>
</tr>
<tr>
<td>Hemoglobin (g /dL)</td>
<td>12.23±1.44</td>
<td>13.06±1.13</td>
<td>0.38</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>38.48±4.13</td>
<td>39.87±3.24</td>
<td>0.32</td>
</tr>
<tr>
<td>MCV(fL)</td>
<td>81.77±7.57</td>
<td>87.21±3.88</td>
<td>0.001</td>
</tr>
<tr>
<td>MCH(pg)</td>
<td>26.10±3.59</td>
<td>28.58±1.99</td>
<td>0.001</td>
</tr>
<tr>
<td>MCHC(gr)</td>
<td>31.76±1.73</td>
<td>32.73±1.19</td>
<td>0.01</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>89.87±87.31</td>
<td>88.13±106.14</td>
<td>0.92</td>
</tr>
<tr>
<td>TIBC(µg/dL)</td>
<td>3.16±64.92</td>
<td>3.24±60.51</td>
<td>0.97</td>
</tr>
<tr>
<td>Free iron (mg /dL)</td>
<td>78.12±13.58</td>
<td>80.82±12.61</td>
<td>0.93</td>
</tr>
<tr>
<td>Total Protein (mg /dL)</td>
<td>7.87±0.76</td>
<td>7.92±0.73</td>
<td>0.76</td>
</tr>
<tr>
<td>Oxidative stress markers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDA(µg/dL)</td>
<td>6.01±12.52</td>
<td>2.8±2.55</td>
<td>0.21</td>
</tr>
<tr>
<td>DPPH(µg/dL)</td>
<td>2.73±0.82</td>
<td>4.84±3.35</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Table 1.

Comparison of mean (± SD) of daily dietary intake, weight and reproductive data between groups

Table 2.

Comparison of mean (± SD) hematological parameters, iron status and serum oxidative stress between groups

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Table 3 displays the frequency and odds ratios of the hematological parameters and variables between groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case group (n=26)</th>
<th>Control group (n=29)</th>
<th>p*</th>
<th>95% CI (OR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC&lt;sup&gt;1&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>low(4.2&lt;)</td>
<td>2(7.6)**</td>
<td>0(0)**</td>
<td>0.12</td>
<td>1.64-2.96(2.20)</td>
</tr>
<tr>
<td>Normal(4.2-5.4)</td>
<td>24(92.4)</td>
<td>29(100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g /dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low(12&lt;)</td>
<td>9(34.6)</td>
<td>7(24.1)</td>
<td>0.55</td>
<td>0.51-5.37(1.66)</td>
</tr>
<tr>
<td>Normal(12-16)</td>
<td>17(65.4)</td>
<td>22(75.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low(37&lt;)</td>
<td>10(38.4)</td>
<td>7(24.1)</td>
<td>0.38</td>
<td>0.61-6.27(1.96)</td>
</tr>
<tr>
<td>Normal(37-47)</td>
<td>16(61.9)</td>
<td>22(75.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCV&lt;sup&gt;2&lt;/sup&gt;(fl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low(90&lt;)</td>
<td>6(23.0)</td>
<td>0(0)</td>
<td>0.006</td>
<td>1.74-3.43(2.45)</td>
</tr>
<tr>
<td>Normal(80-90)</td>
<td>20(77.0)</td>
<td>29(100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCH&lt;sup&gt;3&lt;/sup&gt;(pg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Low(27&lt;)</td>
<td>13(50.0)</td>
<td>5(17.2)</td>
<td>0.01</td>
<td>1.39-16.46(4.8)</td>
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<tr>
<td>Normal(27-31)</td>
<td>13(50.0)</td>
<td>24(82.8)</td>
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</tr>
<tr>
<td>MCHC&lt;sup&gt;4&lt;/sup&gt;(gr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Low(33&lt;)</td>
<td>5(19.2)</td>
<td>1(3.6)</td>
<td>0.09</td>
<td>0.69-59.27(6.4)</td>
</tr>
<tr>
<td>Normal(33-37)</td>
<td>21(80.8)</td>
<td>27(96.4)</td>
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<tr>
<td>Ferritin (μg/dL)</td>
<td></td>
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<tr>
<td>Low(10&lt;)</td>
<td>4(18.2)</td>
<td>2(7.7)</td>
<td>0.39</td>
<td>0.43-16.98(2.6)</td>
</tr>
<tr>
<td>Normal(10-126)</td>
<td>18(81.8)</td>
<td>24(92.3)</td>
<td></td>
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</tr>
<tr>
<td>TIBC&lt;sup&gt;5&lt;/sup&gt;(μg/dL)</td>
<td></td>
<td></td>
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<tr>
<td>Low(250&lt;)</td>
<td>5(20.0)</td>
<td>2(6.9)</td>
<td>0.22</td>
<td>0.59-19.2(3.37)</td>
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<td>Normal(250-450)</td>
<td>20(80.0)</td>
<td>27(93.1)</td>
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<td></td>
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<tr>
<td>Free iron (mg /dL)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Low(37&lt;)</td>
<td>3(11.5)</td>
<td>0(0)</td>
<td>0.09</td>
<td>1.66-3.0(2.26)</td>
</tr>
<tr>
<td>Normal(37-149)</td>
<td>23(88.5)</td>
<td>29(100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Protein (mg /dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low(6.6&lt;)</td>
<td>3(13.0)</td>
<td>1(3.7)</td>
<td>0.32</td>
<td>0.37-40.36(3.9)</td>
</tr>
<tr>
<td>Normal(6.6-8.8)</td>
<td>20(87.0)</td>
<td>26(96.3)</td>
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<tr>
<td>Cancer history</td>
<td></td>
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<tr>
<td>Yes</td>
<td>3(11.5)</td>
<td>6(20.6)</td>
<td>0.71</td>
<td>0.11-2.24(0.5)</td>
</tr>
<tr>
<td>No</td>
<td>23(88.5)</td>
<td>23(94.4)</td>
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<tr>
<td>Iron Supplement (Regularly)</td>
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<tr>
<td>Yes</td>
<td>4(15.3)</td>
<td>14(48.2)</td>
<td>0.01</td>
<td>0.54-0.7(0.19)</td>
</tr>
<tr>
<td>No</td>
<td>22(84.7)</td>
<td>15(51.8)</td>
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<tr>
<td>Menopause</td>
<td></td>
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<tr>
<td>Yes</td>
<td>8(30.7)</td>
<td>9(31.0)</td>
<td>0.6</td>
<td>0.31-3.10(0.98)</td>
</tr>
<tr>
<td>No</td>
<td>18(69.3)</td>
<td>20(69.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Chi-Square Tests; **: N (%)  
<sup>1</sup> Red blood cell count  
<sup>2</sup> Mean corpuscular volume of red cells  
<sup>3</sup> Mean cell hemoglobin  
<sup>4</sup> Mean corpuscular hemoglobin concentration  
<sup>5</sup> Total iron binding capacity

Table 3 shows that the mean iron hematologic parameters, except ferritin, were less in the case group than in the control group. The mean MCV and MCHC were significantly less in the case group than in the control group, indicating microcytic hypochromic anemia, largely caused by iron deficiency (21). This qualitative data cannot be relied upon because of the small sample size, but as observed in Table 3, the percentage of people with mean MCV and MCHC values below normal levels were significantly higher in the case group. Iron supplementation was also significantly higher in the control group than in the case group, and supplements had a protective effect in the control group (CI= 95%; 0.54-0.7); OR= 0.19. The results indicated that the case group showed more serious pathological results in serum iron status than the control group.

**Discussion**

The results showed that the mean iron hematologic parameters, except ferritin, were less in the case group than in the control group. The mean MCV and MCHC were significantly less in the case group than in the control group, indicating microcytic hypochromic anemia, largely caused by iron deficiency (21). This qualitative data cannot be relied upon because of the small sample size, but as observed in Table 3, the percentage of people with mean MCV and MCHC values below normal levels were significantly higher in the case group. Iron supplementation was also significantly higher in the control group than in the case group, and supplements had a protective effect in the control group (CI= 95%; 0.54-0.7; OR= 0.19). The results indicated that the case group showed more serious pathological results in serum iron status than the control group.
Studies have assessed the association of iron consumption with the occurrence of breast cancer and obtained inconsistent results. Studies by Kabat et al. (27, 28) showed no association between iron supplementation and breast cancer, while a study by Kallianpur et al. found that a high intake of heme iron was associated with an increased risk of developing breast cancer in Chinese women (29). In their study, despite the fact that there was no difference between groups in iron, its mean level was higher in the control group than the case group.

Other studies evaluated serum levels of iron. Pavithara et al. (30) evaluated serum levels of some ions in patients with breast cancer and found that the serum level of iron was higher in the case group than in the control group. Jian et al. (20) studied mice under controlled conditions and found that iron deficiency in premenopausal females may be associated with poorer tumor prognosis (20).

Table 3 of the present study demonstrates that most participants were below the age of menopause. Researchers have shown that the risk of mortality and the prevalence of malignant breast cancer are higher in premenopausal women. Although the reasons for this are not clear, one possible cause is iron deficiency, as this problem is very common in premenopausal women (20, 31). Iron is the cofactor of many enzymes, such as propyl 4-hydroxylase, and inhibits this factor by hydroxylation, which induces hypoxia (HIF-1a). In iron deficiency, the inhibitory factor is removed from HIF-1a, and the increase in this substance stimulates the production of vascular endothelial growth factor (VEGF), which is a strong angiogenesis factor in the body. Studies have shown that overexpression of VEGF cells is directly associated with non-estrogen-dependent tumor progression and that serum VEGF levels indicate a higher risk of recurrence and death due to this cancer in patients in the early stages of breast cancer (16).

Although the number of postmenopausal women was roughly equal between groups in the present study, the mean ferritin level was higher in the case group than in the control group. The reason for this is not clear. After menopause, there is an increased risk of iron retention in women (32), and in some studies, a direct correlation has been reported between high levels of ferritin and breast cancer risk (33). It remains unclear whether the cancer results in an increase in ferritin as an acute phase protein, or whether high levels of this protein causes breast cancer (32). Increased ferritin levels are seen more often in post-menopausal women because of iron overload. Iron overload in the body is a prooxidant and can induce oxidative stress and DNA damage. Iron catalyzes Fenton superoxide and hydrogen peroxide (H$_2$O$_2$) produced by aerobic metabolism through the Haber-Weiss reaction to a hydroxyl radical, a strong oxidizing species. Hydroxyl radicals may affect the lipid peroxidation and DNA mutations (16, 32).

The oxidative stress presented in Table 1 shows that the DPPH level (as the total antioxidant capacity index) was significantly higher in the control than in the case group. Although the mean MDA level (as lipid peroxidation) revealed no significant difference between the groups, it was higher in the case group than in the control group. To minimize the effects of therapeutic intervention in this study, blood samples were taken from new cases, but the results emphasize an increase in oxidative stress level markers in the case group compared with the control group.

Oxidative stress is an imbalance between the oxidant and antioxidant reactions that leads to the overexpression of the VEGF gene and the increased metastatic potential of the tumor. The balance between oxidants and antioxidants in the body are controlled by many factors (34, 35). Several studies have assessed the association between phytochemical use and antioxidants and found an inverse association between antioxidant consumption and breast cancer in women (11). Moreover, several studies have also found a significant correlation between serum ferritin level and oxidative stress. Given that a high ferritin level is only one of the factors involved, iron cannot be considered to be the most important factor without measuring other factors in this regard (36).

The present study examined hematologic parameters more extensively than previous studies, while measuring oxidative stress indices. As the selected cases were new cases, the sample size of this study was small, which was a limitation of this study. Thus, it is recommended that future studies be designed with a larger sample size. The scarcity of such studies before the age of menopause and additional factors must be considered when assessing the levels of oxidative stress. In addition, a questionnaire should be designed to assess iron intake from different food sources.

**Conclusion**

The results indicated that iron deficiency anemia is greater in patients with breast cancer than in patients without breast cancer and that iron supplementation appears to have a protective effect against breast cancer incidence. In addition, serum DPPH, as a total antioxidant index, was significantly higher in the control group.

**Acknowledgment**

We would like to thank Shahid Sadoughi University of Medical Sciences for their continued attention and their financial support of this research. We also extend our thanks to the officials and employees of Shahid Sadoughi, Goudarz, Shahid Rahmehoon, and Sayyid al-Shuhada hospitals in Yazd and also thank all the participants whose close cooperation facilitated the completion of this study.

**Funding**

This study was funded by Shahid Sadoughi University of Medical Sciences, Yazd, IR Iran (500 €).

**Conflict of Interests**

The authors declare that they have no competing interests.

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Body iron status, oxidative stress, and breast cancer


