Evaluation of Serum Adiponectin Level in Egyptian Breast Cancer Patients before and after Treatment

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Abstract

Serum adiponectin level was evaluated in thirty five primary breast cancer patients, before and after treatment and ten healthy females with matched age and socioeconomic status, to assess if there is a relation between it and breast cancer, and to find out if it could have a prognostic value. Serum adiponectin level was significantly lower in all and postmenopausal breast cancer patients, before taking any type of treatment, and non-significantly lower in locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy than healthy controls. Non-significant elevations was shown after treatment by surgery, and also after completing treatment by surgery followed by taking 2 cycles of adjuvant chemotherapy followed by treatment by radiotherapy in case of premenopausal locally advanced breast cancer patients. Triglycerides showed significantly high level in all groups of patients. There was statistical negative correlation between serum adiponectin level and body mass index (BMI) in postmenopausal healthy controls, and between serum adiponectin level and BMI, triglycerides in all and postmenopausal breast cancer patients before taking any type of treatment. In conclusion, this study shows that low serum adiponectin level is likely to be associated with increased breast cancer risk, particularly among postmenopausal women. The association between obesity and breast cancer risk might be partly explained by adiponectin.

Key Words: Adiponectin – Breast cancer – Triglycerides – Body mass index – Obesity.

Introduction

IN EGYPT, data reported by Anwar et al. [1] indicated that breast cancer represents 21% of all cancer cases as registered by the Central Cancer Registry in the years 1999/2000 and 1.56 six months of 2001.

Obesity is a well-known risk factor for breast cancer, and obese women are likely to have metastatic breast cancer when they are first diagnosed, and to have a poor prognosis regardless of their menopausal status [2]. Although the exact mechanism remains not to be determined, the hormonal changes associated with obesity are considered to be responsible for this relationship, with particular emphasis being placed on the increased production of estrogen. Adipose tissue is well established as the source of estrogen production through aromatization of androgens which is derived from the adrenal gland [3]. However, the contribution to the development of breast cancer from obesity is not fully explained by increased estrogen levels only [4].

Adipose tissue is not only a passive reservoir for energy storage but is now known to express a variety of metabolites, hormones, and cytokines, known as adipocytokines, which act at both the local and systemic level. These adipocytokines include leptin, adiponectin, complement components, plasminogen activator inhibitor-1 (PAI-1), tumor necrosis factor-α (TNF-α), interleukin (IL)-6, proteins of the renin-angiotensin system (RAS), and resistin [5].

Decreased adiponectin levels are associated with the incidence of breast cancer, but the correlation between serum adiponectin and breast cancer risk is not clear yet, and the molecular basis for the link remains poorly understood [6-8].

In this study, evaluation of serum adiponectin level is estimated in healthy controls and patients suffering from breast cancer before and after treatment, aiming to assess if there is a relation between serum adiponectin level and breast cancer in an attempt to find a new link between obesity and
Subjects and Methods

This study was carried out on thirty five Egyptian females with histopathologically proven primary breast cancer, they were admitted to National Cancer Institute, Cairo University, from Dec 2008 to Jun 2009 and ten healthy females matched in age and socioeconomic status. The patients were with histological types (30 cases invasive duct carcinoma, 1 case invasive lobular carcinoma, 1 case mixed invasive duct and lobular carcinoma, 2 cases tubular carcinoma and 1 case invasive tubular carcinoma), histological grades (3 cases grade I, 31 cases grade II and 1 case grade III) and lymph node metastasis status (27 cases positive and 8 cases negative). All females were divided into 4 groups:

• Group 1: 10 healthy females were considered as a normal control group. This group was subdivided into:
  ° Group 1 (a): 5 premenopausal healthy females.
  ° Group 1 (b): 5 postmenopausal healthy females.

• Group 2: 21 breast cancer patients before taking any type of treatment. This group was subdivided into:
  ° Group 2 (a): 9 premenopausal breast cancer patients. 5 from them were followed-up after treatment by surgery.
  ° Group 2 (b): 12 postmenopausal breast cancer patients. 7 from them were followed-up after treatment by surgery.

• Group 3: 14 locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy. This group was subdivided into:
  ° Group 3 (a): 9 premenopausal locally advanced breast cancer patients. 5 from them were followed-up after completing treatment by surgery followed by taking 2 cycles of adjuvant chemotherapy followed by treatment by radiotherapy.
  ° Group 3 (b): 5 postmenopausal locally advanced breast cancer patients. None of them was followed-up because of their absence after completing treatment.

All the participants were subjected to full history taking and those who found to have diabetes, hypertension, cardio-vascular diseases or history of any type of cancer were excluded from the study. An informed phrasal consent was obtained from each participant and the study was approved by the local committee of Ethics of the Scientific Research of the Faculty of Medicine.

Measurements:

Ten ml venous blood were collected into dry clean tubes after 12 hours overnight fasting. Hemoglobin was determined immediately, the rest was centrifuged at 2000 rpm, serum was stored at −20°C until further analysis.

BMI was calculated according to the WHO standard.

Serum adiponectin was determined using ELISA technique by using an avibion human adiponectin ELISA Kit (Orgenium Laboratories, Helsinki, Finland). Serum triglycerides, total cholesterol, AST, ALT, urea, creatinine and uric acid were determined using colorimetric method. Serum creatinine was determined using buffered kinetic Jaffé reaction without deproteinization method. Hemoglobin was determined using Micros 60 fully automated hematology autoanalyser.

Statistical analysis:

Data were presented as mean ± standard deviation (SD) or number of subjects (n) and percent (%). Simple student t-test was used to compare variables between different groups of patients and healthy controls. Paired t-test was used to compare serum adiponectin level in the same group of patients before and after treatment. Correlation matrix was used to determine the correlation between different variables. Probability (p) <0.05 was considered to be statistically significant. Statistical analysis was performed using statistica version 6.0 software, while the presentations were performed using microsoft excel 2007.

Results

Serum adiponectin level was significantly and non-significantly lower in breast cancer patients before taking any type of treatment (p=0.049) and locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy respectively than healthy controls (Table 1). There was a significantly lower serum adiponectin level in postmenopausal breast cancer patients before taking any type of treatment as compared with those of healthy controls (p=0.033) but this difference did not reach statistical significance in either premenopausal breast cancer patients before taking any type of treatment or pre and postmenopausal locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy as compared with those of healthy controls (Fig. 1).
Table (1): Serum adiponectin levels (µg/ml) in healthy controls, Breast cancer patients before taking any type of treatment and locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy.

<table>
<thead>
<tr>
<th></th>
<th>Healthy control Mean±SD</th>
<th>Breast cancer patients before taking any type of treatment Mean±SD</th>
<th>p</th>
<th>Locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy Mean±SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=10</td>
<td>n=21</td>
<td></td>
<td>n=14</td>
<td></td>
</tr>
<tr>
<td>*All</td>
<td>19.37±1.13</td>
<td>18.13±1.75</td>
<td>0.049</td>
<td>18.13±2.15</td>
<td>0.111</td>
</tr>
<tr>
<td>Premenopause</td>
<td>n=5</td>
<td>n=9</td>
<td>0.763</td>
<td>n=9</td>
<td>0.262</td>
</tr>
<tr>
<td>18.83±1.34</td>
<td>18.60±1.37</td>
<td>17.46±2.38</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopause</td>
<td>n=5</td>
<td>n=12</td>
<td>0.033</td>
<td>n=5</td>
<td>0.284</td>
</tr>
<tr>
<td>19.90±0.59</td>
<td>17.77±1.96</td>
<td></td>
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</tr>
</tbody>
</table>

When p-value <0.05, it is statistically significant. 
*All = Premenopausal + postmenopausal.

Non-significant elevation was shown in breast cancer patients before taking any type of treatment and after treatment by surgery, and there was also a non-significant elevation in serum adiponectin level in pre and postmenopausal patients before taking any type of treatment and after treatment by surgery, but in postmenopausal patients the elevation was nearly significant (p=0.064) (Table 2). In premenopausal locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy and after completing treatment by surgery followed by taking 2 cycles of adjuvant chemotherapy followed by treatment by radiotherapy, the level was also non-significantly elevated (Figs. 2,3).

There was no significant difference between either breast cancer patients before taking any type of treatment or locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy and healthy controls with respect to serum levels of total cholesterol, AST, ALT, urea, creatinine, uric acid and hemoglobin. Only triglycerides showed a significantly higher level in breast cancer patients before taking any type of treatment (p=0.000) and locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy (p=0.001) as compared with healthy controls. Both pre and postmenopausal breast cancer patients before taking any type of treatment (p=0.008, p=0.029 respectively) and pre and postmenopausal locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy (p=0.021, p=0.006 respectively) showed also a significantly higher level as compared to those of healthy controls.
Table (2): Serum adiponectin levels (µg/ml) in breast cancer patients before taking any type of treatment and at (20-30) days after treatment by surgery, and in premenopausal locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy and after completing treatment by surgery followed by taking 2 cycles of adjuvant chemotherapy followed by treatment by radiotherapy.

<table>
<thead>
<tr>
<th></th>
<th>Breast cancer patients before taking any type of treatment Mean±SD</th>
<th>Locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before surgery</td>
<td>After surgery</td>
</tr>
<tr>
<td>All</td>
<td>n=12</td>
<td>n=12</td>
</tr>
<tr>
<td>Premenopause</td>
<td>18.50±1.53</td>
<td>18.75±1.55</td>
</tr>
<tr>
<td>Postmenopause</td>
<td>18.40±1.71</td>
<td>18.74±1.93</td>
</tr>
</tbody>
</table>

When p-value <0.05, it is statistically significant.

Fig. (2): Serum adiponectin level (µg/ml) in breast cancer patients before taking any type of treatment and at (20-30) days after treatment by surgery.

Fig. (3): Serum adiponectin level (µg/ml) in premenopausal locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy and after completing treatment by surgery followed by taking 2 cycles of adjuvant chemotherapy followed by treatment by radiotherapy.
Table (3): Correlation between serum adiponectin level (µg/ml) and BMI (kg/m²) in healthy controls, breast cancer patients before taking any type of treatment and locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy.

<table>
<thead>
<tr>
<th></th>
<th>Adiponectin (µg/ml) Mean±SD</th>
<th>BMI (kg/m²) Mean±SD</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Healthy control:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (n=10)</td>
<td>19.37±1.13</td>
<td>30.24±3.54</td>
<td>-0.59</td>
<td></td>
</tr>
<tr>
<td>Premenopause (n=5)</td>
<td>18.83±1.34</td>
<td>29.93±4.16</td>
<td>-0.70</td>
<td>0.074</td>
</tr>
<tr>
<td>Postmenopause (n=5)</td>
<td>19.90±0.59</td>
<td>30.54±3.26</td>
<td>-0.92</td>
<td>0.187</td>
</tr>
<tr>
<td><strong>Breast cancer patients before taking any type of treatment:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (n=21)</td>
<td>18.13±1.75</td>
<td>31.90±5.70</td>
<td>-0.62</td>
<td></td>
</tr>
<tr>
<td>Premenopause (n=9)</td>
<td>17.77±1.96</td>
<td>33.61±6.01</td>
<td>-0.31</td>
<td>0.413</td>
</tr>
<tr>
<td>Postmenopause (n=12)</td>
<td></td>
<td></td>
<td></td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (n=14)</td>
<td>18.13±2.15</td>
<td>29.85±5.00</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Premenopause (n=9)</td>
<td>17.46±2.38</td>
<td>28.58±4.63</td>
<td>0.37</td>
<td>0.127</td>
</tr>
<tr>
<td>Postmenopause (n=5)</td>
<td>19.33±0.95</td>
<td>32.14±5.30</td>
<td>0.28</td>
<td>0.324</td>
</tr>
</tbody>
</table>

When p-value <0.05, it is statistically significant.

Table (4): Correlation between serum adiponectin level (µg/ml) and serum triglycerides level (mg/dl) in healthy controls, breast cancer patients before taking any type of treatment and locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy.

<table>
<thead>
<tr>
<th></th>
<th>Adiponectin (µg/ml) Mean±SD</th>
<th>Triglycerides (mg/dl) Mean±SD</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Healthy control:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (n=10)</td>
<td>19.37±1.13</td>
<td>74.54±20.15</td>
<td>0.03</td>
<td>0.925</td>
</tr>
<tr>
<td>Premenopause (n=5)</td>
<td>18.83±1.34</td>
<td>68.22±17.14</td>
<td>-0.79</td>
<td>0.114</td>
</tr>
<tr>
<td>Postmenopause (n=5)</td>
<td>19.90±0.59</td>
<td>80.87±22.81</td>
<td>0.85</td>
<td>0.068</td>
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<tr>
<td><strong>Breast cancer patients before taking any type of treatment:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (n=21)</td>
<td>18.13±1.75</td>
<td>120.34±32.50</td>
<td>-0.51</td>
<td>0.017</td>
</tr>
<tr>
<td>Premenopause (n=9)</td>
<td>18.60±1.37</td>
<td>124.86±37.27</td>
<td>-0.48</td>
<td>0.191</td>
</tr>
<tr>
<td>Postmenopause (n=12)</td>
<td>17.77±1.96</td>
<td>116.95±29.67</td>
<td>-0.66</td>
<td>0.020</td>
</tr>
<tr>
<td><strong>Locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (n=14)</td>
<td>18.13±2.15</td>
<td>137.71±47.72</td>
<td>-0.20</td>
<td>0.488</td>
</tr>
<tr>
<td>Premenopause (n=9)</td>
<td>17.46±2.38</td>
<td>140.77±58.72</td>
<td>-0.17</td>
<td>0.666</td>
</tr>
<tr>
<td>Postmenopause (n=5)</td>
<td>19.33±0.95</td>
<td>132.20±21.16</td>
<td>-0.38</td>
<td>0.529</td>
</tr>
</tbody>
</table>

When p-value <0.05, it is statistically significant.

**Discussion**

Relationship of obesity to some forms of cancer has been known for a long time [9], it is not surprising that researchers were trying to discover the possible role of adipocytokines in the regulation of carcinogenesis as a link between obesity and cancer [10]. Obesity is an established risk factor for breast cancer, with an estimated 50% increased risk for obese compared with normal-weight women [11].

This study shows that there was a statistical negative correlation between serum adiponectin level and BMI in postmenopausal healthy controls, breast cancer patients before taking any type of treatment and postmenopausal breast cancer patients before taking any type of treatment. These findings are in agreement with Miyoshi et al. [6]; Chen et al. [8]; Arita et al. [12]; Hotta et al. [13]; Yang et al. [14]; Diab et al. [15]; Hou et al. [16] who reported that serum adiponectin levels are inversely related to BMI. However, Kang et al. [17] found no significant correlation between serum adiponectin level and BMI.

The studied serum adiponectin level was significantly lower in breast cancer patients before
taking any type of treatment than healthy controls, and there was a significantly lower serum adiponectin level in postmenopausal patients as compared with those of healthy controls but this difference did not reach statistical significance in premenopausal patients as compared with those of healthy controls. These results are in agreement with previous studies which demonstrated that serum adiponectin levels were significantly decreased in breast cancer patients in comparison to controls \cite{6,8,16,18}, and there was a significant difference in serum adiponectin levels between postmenopausal patients and controls, but no difference was found between premenopausal patients and controls \cite{16}. Diab et al. \cite{15} observed that there was a significant decrease of adiponectin in postmenopausal breast cancer patients with metastasis than controls, although Chen et al. \cite{8} found that menopausal status did not affect serum adiponectin levels. However Kang et al. \cite{17} showed that serum adiponectin level was lower in breast cancer patients than controls, but this difference did not reach statistical significance and when serum adiponectin levels were compared in cases and controls according to menopausal status, there was no significant difference in serum adiponectin levels between cases and controls in either pre or postmenopausal women.

Miyoshi et al. \cite{6}; Chen et al. \cite{8}; Hou et al. \cite{16}; Körner et al. \cite{18} suggested that low serum adiponectin levels are significantly associated with an increased risk for breast cancer. Miyoshi et al. \cite{6} showed that such an association was observed both in pre and postmenopausal women, however Mantzoros et al. \cite{7}; Tworoger et al. \cite{19} found an inverse association of adiponectin levels with breast cancer risk among postmenopausal women and no such association between adiponectin levels and breast cancer risk among premenopausal women. Körner et al. \cite{18} illustrated that such an association was particularly among premenopausal and obese women.

Miyoshi et al. \cite{6}; Hou et al. \cite{16} demonstrated that low serum adiponectin levels were associated with high histological grade, large tumor size \cite{6} and lymph nodes metastasis of breast cancer \cite{16,17}.

In this study, also serum adiponectin level was lower in locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy than healthy controls, but this difference did not reach statistical significance, and there was also a non-significantly lower serum adiponectin level in pre and postmenopausal patients as compared with those of healthy controls. These results demonstrate that serum adiponectin level in all and postmenopausal locally advanced breast cancer patients after treatment by neoadjuvant chemotherapy was non-significantly low although the level in all and postmenopausal breast cancer patients before taking any type of treatment was significantly low.

When we compared serum adiponectin level in breast cancer patients before taking any type of treatment and at (20-30 days) after treatment by surgery, the level was elevated, but this difference did not reach statistical significance. There was also a non-significant elevation in serum adiponectin level in pre and postmenopausal patients before taking any type of treatment and after treatment by surgery but in postmenopausal patients the elevation was nearly significant. When we compared serum adiponectin level in locally advanced premenopausal breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy and after completing treatment by surgery followed by taking 2 cycles of neoadjuvant chemotherapy followed by radiotherapy, the level was elevated but this difference also did not reach statistical significance. These results may possibly be due to two reasons: The first is the removal of breast adipose tissue during surgery which lead to the reduction of the total amount of body adipose tissue so serum adiponectin level was increased again, and the second is that breast cancer cells may affect on adiponectin synthesis and/or secretion so the therapeutic effect of neoadjuvant chemotherapy or the removal of breast cancer cells by surgery only or by surgery followed by adjuvant chemotherapy followed by radiotherapy caused serum adiponectin level to be increased again.

It has been reported that obesity-related breast cancer is more often ER positive than is the general case, but this has not been a consistent finding \cite{20}. Kang et al. \cite{17} also showed that the frequency of the tumors with negative ER was significantly increased in the patients with less than the median adiponectin level. However, in the previous study, the status of ER and PR did not affect the adiponectin levels in breast cancer patients, and no significant correlation was observed between the serum adiponectin and estrogen levels in postmenopausal women \cite{6,8}, implying that adiponectin may influence the development of breast cancer through other pathways.

One possible mechanism explaining associations between obesity and cancer other than estrogen is hyperinsulinemia or insulin resistance. Insulin enhances the activity of IGF-1, and high
levels of circulating IGF-1 are correlated with risk of development of breast cancer [21]. However, Mantzoros et al. [7] reported that associations between serum adiponectin and breast cancer risk were independent of possible effects of major components of the IGF system, leptin, and BMI.

The molecular mechanism of the contributions of low serum adiponectin levels to carcinogenesis and progression of tumor is currently unknown. Recently, adiponectin has been reported to induce activation of caspase enzymes which leads to EC apoptosis, and the reduction of tumor neovascularization [22]. In addition, adiponectin has a direct inhibitory effect on proliferation of VSMCs and myelomonocytic progenitors [23]. In one study, adiponectin has been reported to induce growth arrest and apoptosis of MDA-MB-231 breast cancer cells [24]. These results are speculated to infer that adiponectin may promote apoptosis directly by activation of apoptotic enzymes in the caspase cascade or modulation of expression of apoptosis-related genes [17].

Adiponectin plays an important role in glucose metabolism [25-28], and a decrease in the serum adiponectin levels is shown to be associated with an increase in the glucose levels [13]. It is believed that high glucose levels stimulate the proliferation of cultured breast cancer cells [29], when these observations were taken together, it is speculated that adiponectin modulates the breast cancer risk through affecting the glucose metabolism [6].

Takahata et al. [30] showed that AdipoR1 and AdipoR2 were expressed in both normal breast ECs and breast cancer cells; Dieudonne et al. [31] reported that MCF-7 cells expressed adiponectin receptors and responded to adiponectin by reducing their growth, AMPK activation, and p42/p44 MAPK inactivation. Those findings indicated that adiponectin might inhibit the proliferation of breast cancer cells directly through binding to adiponectin receptors [16].

We found no significant differences between either breast cancer patients before taking any type of treatment (all patients, pre or postmenopausal patients) or locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy (all patients, pre or postmenopausal patients) and healthy controls. Similar results have been reported by Hou et al. [16]; Gaard et al. [32]; Agurs-Collins et al. [33] who observed no significant differences in total cholesterol levels between breast cancer patients and controls. However, these results were inconsistent with Ferraroni et al. [34]; Ray et al. [35] who suggested that serum cholesterol was significantly higher in breast cancer patients than controls, Abu-Bedair et al. [36] found that total cholesterol levels significantly increased in pre-menopausal patients with no significant change in postmenopausal women.

Triglycerides showed a significantly higher level in breast cancer patients before taking any type of treatment (all patients, pre or postmenopausal patients) and locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy (all patients, pre or postmenopausal patients) as compared to those of healthy controls. These findings are supported by Hou et al. [16]; Agurs-Collins et al. [33]; Ray et al. [35]; Potischman et al. [37]; Kökoglu et al. [38]; Schreier et al. [39] who have shown that breast cancer patients had significantly higher triglycerides levels compared to controls. Also Hou et al. [16]; Abu-Bedair et al. [36] found a significantly higher triglycerides levels in postmenopausal breast cancer patients as compared to controls but could not find this in pre-menopausal breast cancer patients. Breast cancer patients with advanced disease have a significantly higher serum triglycerides levels than patients with less advanced disease [33,38,40].

Regarding the serum total cholesterol level, there were no significant differences between breast cancer patients before taking any type of treatment (all patients, pre or postmenopausal patients), locally advanced breast cancer patients after treatment by 4 cycles of neoadjuvant chemotherapy (all patients, pre or postmenopausal patients) and healthy controls. Similar results have been reported by Hou et al. [16]; Gaard et al. [32]; Agurs-Collins et al. [33] who observed no significant differences in total cholesterol levels between breast cancer patients and controls. However, these results were inconsistent with Ferraroni et al. [34]; Ray et al. [35] who suggested that serum cholesterol was significantly higher in breast cancer patients than controls, Abu-Bedair et al. [36] found that total cholesterol levels significantly increased in pre-menopausal patients with no significant change in postmenopausal women.

The significant correlation between the high levels of triglycerides and breast cancer risk may be attributed to differences in lipid metabolism among breast cancer cases and controls, and this is further supported by the association between increasing levels of triglycerides and advancing stages of the disease [33]. The etiology of altered lipids and lipoproteins seen among cancer patients may involve more than one mechanism. Takatani et al. [41] suggested that elevated levels of triglycerides are associated with a decreased level of SHBG, resulting in increased amounts of free estradiol and increased breast cancer risk. Another mechanism could be related to the association of insulin resistance with hypertriglyceridemia and breast cancer risk [42,43]. Obesity that is related to
insulin resistance may be a factor associated with an altered lipid metabolism. It has also been postulated that hypertriglyceridemia may be the result of decreased triglyceride clearance from plasma. This may be due to inhibition of LPL activity resulting in impaired catabolism of VLDL cholesterol, increased serum triglyceride levels and a decrease in HDL-cholesterol levels [44,45].

We also found that there was a statistical negative correlation between serum adiponectin level and serum triglycerides level in breast cancer patients before taking any type of treatment and postmenopausal breast cancer patients before taking any type of treatment and these results are in agreement with Hou et al. [16]. Matsubara et al. [46]; Baratta et al. [47] who found that serum adiponectin levels showed a negative correlation with triglycerides. Adiponectin lower free fatty acid levels via an increase of muscle free fatty acid oxidation resulting in a modulation of triglyceridemia and glycemia [26]. Adiponectin reduces lipids by inhibiting hepatic lipogenesis [48]. Baratta et al. [47] suggested that adiponectin levels directly regulate lipid metabolism and that this effect is independent of the patient fat mass, weight loss, and insulin sensitivity.

In conclusion, this study suggests that low serum adiponectin level is likely to be associated with increased breast cancer risk, particularly among postmenopausal women. Adiponectin could be considered as a biomarker for breast cancer development in obesity and the association between obesity and breast cancer risk might be partly explained by adiponectin.

Obese women, particularly postmenopausal women, should be encouraged to lose weight as a suggested method to decrease their risk of breast cancer.

Further studies with larger number of subjects and large-scaled prospective studies should be supported in the future. A study about the precise mechanism of the relationship of adiponectin and breast cancer, as well as its potential diagnostic, prognostic and/or therapeutic utility, requires further investigations.

References


