The Role of Adiponectin Hormone and some Biochemical Parameters in Women with Invasive Ductal Carcinoma of the Breast in Thi-Qar Province-Iraq

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Abstract:
Breast cancer is the most frequently diagnosed cancer and is a common cause of cancer related death in women, accounting for 25% of cancer cases and 15% of cancer-related deaths worldwide. The present study was designed to determine and compare the levels of Adiponectin hormone, Vitamin D3, Calcium, Alkaline phosphatase, and C-reactive protein among women with Invasive ductal carcinoma and healthy individuals. The study was designed to determine and compare the levels of serum Adiponectin hormone, Vitamin D3, Calcium, Alkaline phosphatase, and C-reactive protein levels were measured in eighty-five patients with Invasive ductal carcinoma and seventy-five supposed healthy subjects. The levels of serum Adiponectin hormone, Vitamin D3, were revealed significant decrease among patients with Invasive ductal carcinoma as compared to control group whereas the levels of Calcium, Alkaline phosphatase, and C-reactive protein showed a significant increase in Invasive ductal carcinoma patients in comparison to control subjects (P ≤ 0.05). This present study indicated that low blood adiponectin level was associated with the risk of obesity-related malignancies, including breast cancer, we can conclude that deficient of vit. D3 may contribute to the process of carcinogenesis among the breast cancer patients, and our findings revealed significant in Calcium, Alkaline phosphatase, and C-reactive protein levels among patients with Invasive ductal carcinoma.

Keywords: Breast cancer, Invasive ductal carcinoma, Adiponectin hormone, Vitamin D3, Calcium, Alkaline phosphatase, and inflammatory marker C-reactive protein.

INTRODUCTION:
Breast cancer is the most frequently diagnosed cancer and is a common cause of cancer related death in women, accounting for 25% of cancer cases and 15% of cancer-related deaths worldwide (Torre L. et al., 2017). Invasive ductal carcinoma which is the most common type comprises 50-75% of all breast cancers (Dillon D. et al., 2010). The circulating adiponectin levels are inversely associated with the risk of obesity-related malignancies, including breast cancer (Tworoger S. et al., 2007). Low blood concentrations of adiponectin are associated with high incidence and poor prognosis of breast cancer (Fu Y. et al., 2005). Vitamin D deficiency is also associated with secondary elevation in Para thyroid hormone (PTH) serum levels which has carcinogenic and tumor promoting effects. Hence, may lead to an increased risk of breast cancer (Hoey R. et al., 2003). Calcium is involved in many cellular process including those involved in the process of carcinogenesis, as gene transcription, cell motility, angiogenesis, calcium regulates various cellular processes, including those
relevant to tumorgenesis, such as cell motility, angiogenesis, gene transcription, apoptosis and proliferation (Dickinson H. \textit{et al.}, 2006).

Increase serum level of elevated activity of alkaline phosphatase (ALP) in patients with malignancies including metastatic breast cancer (Ijaz A. \textit{et al.}, 2006).

Researchers proposed that serum C-reactive protein (CRP) could be a marker of increased risk for breast cancer, estimation of CRP can be looked at as a simple, cost effective, easily available screening test to assess future risk of breast cancer (Guo L. \textit{et al.}, 2015).

\textbf{MATERIALS AND METHODS}

The current study is a kind of prospective study. The samples are obtained from the patients who participated in specialist clinics and the oncology center in Al-Habooby Hospital. The eighty-five samples of blood were obtained from the patients of invasive ductal carcinoma, and seventy-five samples of blood were obtained from normal women as a control group. Around five milliliters of blood was obtained and permitted to clot at normal temperature for ten minutes in hollow disposable centrifuge tubes for the separation in a centrifuge at 3000 xg.

The samples of serum were stored and separated at the temperature of minus twenty-degree centigrade before analyzing for Adiponectin hormone, vitamin D3, Calcium, Alkaline phosphatase, and C-reactive protein. The enzyme linked immunoassay technique was used to estimate serum Adiponectin using ELISA Reader. The kit was provided by Elabscience which is located in the USA.

The sandwich immune detection method was used to estimate serum vit.D3 and CRP using I chroma™. The kit was provided by Boditech, Korea.

The enzymatic colorimetric method by (UV/VIS spectrophotometer) analyzed Serum Calcium, and the kit was provided by Biolabo, France.

The enzymatic colorimetric method by (UV/VIS spectrophotometer) analyzed Serum Alkaline phosphatase (ALP), and the kit was provided by Biomerieux, France.

The results of the experiment are presented in the form of mean ± standard deviations. The parameters in various studied groups were compared using one-way ANOVA-test. The P-values (P \leq 0.05) were taken very significant in this regard.

\textbf{RESULTS}

In this work, we determined the effect of this disease on the Adiponectin hormone, vitamin D3, Calcium, Alkaline phosphatase, and C-reactive protein. ADP hormone, vitamin D3 were showing a significant decrease in the patients of invasive ductal carcinoma in comparison to the control group. Calcium, ALP, and CRP were showing a significant increase in the patients of invasive ductal carcinoma in comparison to the control group.
<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>ADP levels (ng/ml) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>75</td>
<td>6.74±1.69&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>patients</td>
<td>85</td>
<td>0.50±0.11&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Note:** Each value represents mean ± SD values with non-identical superscript (a, b or c…etc.), were considered significantly differences (P≤ 0.05).

- **No:** Number of subjects.
- **SD:** Standard deviation.

### Table (2): Serum Vit. D3 levels of control and invasive ductal carcinoma

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Vit D3 levels (nmol/L) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>75</td>
<td>30.50±2.40&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>patients</td>
<td>85</td>
<td>21.98±1.20&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

-Legend as in table (1).

### Table (3): Serum Calcium levels of control and invasive ductal carcinoma

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Calcium levels (mmol/L) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>75</td>
<td>2.27±0.11&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>patients</td>
<td>85</td>
<td>2.73±0.19&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

-Legend as in table (1).

### Table (4): Serum ALP activity of control and invasive ductal carcinoma

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>ALP activity (U/L) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>75</td>
<td>67.32±13.84&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>patients</td>
<td>85</td>
<td>132.89±21.50&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

-Legend as in table (1).

### Table (5): Serum CRP levels of control and invasive ductal carcinoma

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>CRP levels (mg/L) Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>75</td>
<td>6.84±1.76&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>patients</td>
<td>85</td>
<td>11.81±1.18&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

-Legend as in table (1).
DISCUSSION:
Invasive tumors spread from the original site (either milk duct or lobules) into surrounding tissue of the breast and may spread to lymph nodes and/or other parts of body (Dillon D. et al., 2010; Merajver S. et al., 2010).

Our finding agree with (Ahmed S. et al., 2015) studied 175 diagnosed breast cancer patients and 175 healthy controls. They found serum adiponectin was significantly decreased in breast cancer cases when compared to control subjects, had a statistically significant difference (P<0.05). Several studies have demonstrated that low serum adiponectin levels are associated with increased risk for breast cancer (Chlebowski R. et al., 2005; Mohan R. et al., 2012; and Hdeel R. et al., 2019). Obesity is significantly associated with hypoadiponectinemia agrees with a study done by (Haluzik M. et al., 2004). Laboratory studies have demonstrated that vitamin D3 and its analogs inhibit cell proliferation and promote apoptosis in cancer cells (Sergeev I., 2012; Balasubramanian S. and Rotti S., 2013). Calcium are strongly correlated and share similar anti-carcinogenic effects on mammary gland. Hence, any apparent effect of vitamin D on breast cancer risk might be due in part to an effect of calcium and vice versa. However, few epidemiologic studies have investigated the joint and independent effects of vitamin D and calcium on breast cancer risk (McCullough M. et al., 2005).

The progressive increase in the serum alkaline phosphatase (ALP) activity in breast cancer patients is an indication of metastasis (Ramaswamy G. et al., 2000; Mishra S. et al., 2004).

Elevation of serum ALP occurs because of the accelerated denovo synthesis of the enzyme and subsequent regurgitation into the serum, the serum alkaline phosphatase level is a better predictor for metastatic breast cancer in comparison to other parameters activities as its level gradually increases as the stages advances. CRP is an important biomarker of chronic inflammatory processes that may explain health challenges among women following breast cancer diagnosis, for example, higher CRP levels have been implicated in reduced disease-free survival and higher risk of mortality among breast cancer patients (Allin K. et al., 2011; Villaseñor A. et al., 2014). Epidemiological prospective study proved CRP as a well-established independent prognostic marker in breast cancer (Sicking I. et al., 2014).

CONCLUSIONS:
The data provided in this study helped to reach the below conclusions:
1- This present study indicated that low serum adiponectin level was associated with the risk of obesity-related malignancies, including breast cancer.
2- Based on the findings in this study, especially low levels of vit.D3, we can conclude that deficient of vit.D3 may contribute to the process of carcinogenesis among the breast cancer patients.
3- Serum calcium levels were positively associated with breast cancer risk in premenopausal and/or overweight women.
4- An increase in alkaline phosphatase activity was found in sera with patients with invasive ductal carcinoma.
5- A clear relationship between elevated CRP levels and prognoses indicates that CRP could be useful in predicting prognoses in advanced cancer patients.
REFERENCES:


