The relationship between vitamin D with breast cancer

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ABSTRACT

Objective: Evaluate the association between vitamin D2 with breast cancer (BC). Methods: A case control study department of oncology, Salahaddin Hospital, during the period from July 2019 to January 2020. Data were obtained from 90 participants, 58 women with BC and 30 women as healthy control. The BC women were further subdivided into 20 women with chemotherapy (G1), 14 women received less than 6 doses of chemotherapy (G2), 15 women received more than 6 doses of chemotherapy (G3), 9 women received chemoradiation therapy (G4). Results: Vitamin D in all BC women was significantly lower compared to healthy control (25.36±5.53 ng/L), additionally it was lower in G1 (8.48±1.97 ng/L) compared to G4 (14.29±2.69 ng/L), G3 (9.52±2.59 ng/L) was lower...
compared to G4, no difference was observed between G1, G2 (10.35±2.83 ng/L), and G3. Conclusions: there is clear inverse association between vitamin D with breast cancer, especially in those with early BC compared to more advance cases.

Keywords: vitamin D, breast cancer, inverse relationship

1. INTRODUCTION

Vitamin D is water insoluble vitamin with an important role in the regulation of calcium of phosphate metabolism. Multiple studies established the association between this vitamin with several disease including solid tumors like breast (Garland et al., 2006). In the female breast cancer (BC) considered the most prevalent cancer which represent 33.8% of all female cancer in Iraq (Al-Hashimi and Wang, 2014). Some indicate a relationship between dietary components with BC (Doll and Peto, 1981). Vitamin D is the precursor of 1,25-dihydroxyvitamin D (D3) in cells, this active form affects various metabolic pathways some of which can trigger cancer, it has two active forms D2 and D3. D3 can act as protector of against cancer through induction of apoptosis, stimulation of cell differentiation, anti-inflammatory and antiproliferative effects and inhibition of angiogenesis, invasion and metastasis (Feldman et al., 2014; Al-Radeef et al., 2019). The current work aims to evaluate the association between levels of vitamin D with breast cancer at various stages of treatment.

2. PATIENTS AND METHODS

A case control study department of oncology, Salahaddin Hospital, during the period from 22th August 2019 to 25th November 2019. Data were obtained from 88 participants, 58 women with BC and 30 women as healthy control. The BC women were further subdivided into 20 women with chemotherapy (G1), 14 women received less than 6 doses of chemotherapy (G2), 15 women receive more than 6 doses of chemotherapy (G3), 9 women received chemoradiation therapy (G4).

A 5 ml venous blood was obtained from each participant, then the sample were centrifuged for 10 minutes (3,000 rpm) and sera was obtained and stored at (-37 C) for further analysis. Vitamin D was measured using solid phase ELISA technique (Calbiotech, USA), this method measure the active form of vitamin D i.e. 25 (OH) vitamin D (D2). The rest of the parameters measured using ELISA, CA 15-3 (Calbiotech, USA), estrogen (Calbiotech, USA), AST, ALT (Randox, England) and ALP (Biolabo, France) according to the manufacturer instruction.

3. RESULTS

Vitamin D in all BC women was significantly lower compared to healthy control, additionally it was lower in G1 compared to G4, G3 was lower compared to G4, no difference was observed between G1, G2, and G3. The rest of variables are illustrated in table 1.

Figure 1 assessment of vitamin D in various groups
Table 1: assessment of laboratory parameters in BC and healthy control

<table>
<thead>
<tr>
<th>Variables</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>20</td>
<td>14</td>
<td>15</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>Vitamin D (ng/L)</td>
<td>8.48 ± 1.97&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10.35 ± 2.83&lt;sup&gt;b&lt;/sup&gt;</td>
<td>9.52 ± 2.59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.29 ± 2.69&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25.36 ± 5.53&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>CA 15-3 (U/ml)</td>
<td>176.74 ± 33.16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20.16 ± 5.09&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17.32 ± 2.98&lt;sup&gt;b&lt;/sup&gt;</td>
<td>19.22 ± 2.55&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16.94 ± 3.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>E2 (pg/ml)</td>
<td>66.85 ± 16.84&lt;sup&gt;a&lt;/sup&gt;</td>
<td>71.93 ± 15.65&lt;sup&gt;b&lt;/sup&gt;</td>
<td>73.12 ± 14.65&lt;sup&gt;b&lt;/sup&gt;</td>
<td>86.0 ± 11.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>68.2 ± 11.79&lt;sup&gt;bc&lt;/sup&gt;</td>
</tr>
<tr>
<td>AST (U/l)</td>
<td>14.09 ± 4.83&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.15 ± 3.67&lt;sup&gt;ac&lt;/sup&gt;</td>
<td>11.68 ± 3.02&lt;sup&gt;ac&lt;/sup&gt;</td>
<td>18.79 ± 2.16&lt;sup&gt;b&lt;/sup&gt;</td>
<td>9.25 ± 2.29&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>12.48 ± 2.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.3 ± 2.18&lt;sup&gt;bc&lt;/sup&gt;</td>
<td>10.54 ± 1.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>13.93 ± 2.01&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.59 ± 1.76&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>ALP (U/l)</td>
<td>49.46 ± 9.69&lt;sup&gt;ac&lt;/sup&gt;</td>
<td>60.26 ± 7.86&lt;sup&gt;abc&lt;/sup&gt;</td>
<td>47.06 ± 12.1&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>68.17 ± 16.63&lt;sup&gt;bc&lt;/sup&gt;</td>
<td>56.5 ± 10.87&lt;sup&gt;bc&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Variables share same letter indicate there is no significant difference.
Data presented using their mean ± standard deviation.

There was inverse significant relationship between vitamin D with CA 15-3 in the following groups G1, G2, and G3 while it becomes direct significant in G4 groups. ALT showed inverse significant relationship with vitamin D in G1, G2 and G4 groups (figure 1). AST showed inverse significant relationship with vitamin D in G4 only, while ALP showed direct significant relationship with vitamin D in G4 only, as illustrated in table 2.

Table 2: relationship between vitamin D with other laboratory parameters in various BC patients

<table>
<thead>
<tr>
<th>Vitamin D</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA 15-3</td>
<td>r = -0.444</td>
<td>p-value = 0.050</td>
<td>-0.694</td>
<td>p-value = 0.006</td>
<td>-0.546</td>
</tr>
<tr>
<td>E2</td>
<td>r = -0.351</td>
<td>p-value = 0.129</td>
<td>-0.144</td>
<td>p-value = 0.624</td>
<td>0.337</td>
</tr>
<tr>
<td>AST</td>
<td>r = -0.288</td>
<td>p-value = 0.218</td>
<td>-0.161</td>
<td>p-value = 0.582</td>
<td>0.073</td>
</tr>
<tr>
<td>ALT</td>
<td>r = -0.448</td>
<td>p-value = 0.048</td>
<td>-0.788</td>
<td>p-value = 0.001</td>
<td>-0.200</td>
</tr>
<tr>
<td>ALP</td>
<td>r = -0.270</td>
<td>p-value = 0.250</td>
<td>0.035</td>
<td>p-value = 0.226</td>
<td>-0.315</td>
</tr>
</tbody>
</table>

Linear regression analysis, r: regression coefficient (standardized beta).

4. DISCUSSION
In the present study vitamin D showed significantly lowered value in BC groups compared to healthy control (table 1). This was in agreement with previous studies in which they found inverse relationship between vitamin D with BC, like Chen et al. OR = 0.55, 95% CI = 0.38-0.80 (Chen et al., 2010), Bauer et al. with a step-wise inverse correlation observed if vitamin D is >27 ng/mL (Bauer et al., 2013), Mohr et al. in which vitamin D >47 ng/ml associated with 50% lower risk of BC (Mohr et al., 2011), and others (Ordonez-Mena et al., 2016, Bilinski and Boyages, 2013, Shekarriz-Foumani and Khodaie, 2016, Mohammed et al., 2019).

Various theories can explain this inverse association, changes in vitamin D receptor (VDR) in BC tissues and cells compared to normal cells, in which they found VDR had considerable heterogeneity at transcript level (Saccone et al., 2015), to VDR dysregulation in response to oncogene expression in BC tissue (Kemmis and Welsh, 2008), and less sensitivity of VDR to 2(OH)D in BC (Kemmis and Welsh, 2008).

5. CONCLUSION
There is clear inverse association between vitamin D with breast cancer, especially in those with early BC compared to more advance cases. This indicate low vitamin D2 increase risk of breast cancer.

Author contribution
Eman Taha Hamdi: Conception and design of the work, the acquisition, analysis, and interpretation of data for the work, and Drafting the work.
Abdulsalam Tawfeeq Alsamarai: Conception and design of the work, interpretation of data for the work, and revising it critically for important intellectual content
Ali Abbas Ali: Conception and design of the work, and Drafting the work and finally revising it critically for important intellectual content.
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Conflict of Interest
The authors declare that they have no conflict of interest.

Informed consent
Written informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval for human
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 (Code: 2019/B115).

REFERENCE