

Study Association of CA15-3, CEA with Vitamin D3 in Patients Suffering from Breast Cancer

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ABSTRACT

Background: The study aims to determine the relationship between CEA and CA15-3 with Vitamin D3 among breast cancer patients. **purpose:** The study aims to explore the relationship between CEA and CA15-3 with Vitamin D3 in breast cancer patients and hypothesizes that Vitamin D3 may influence these biomarkers related to cancer prognosis. **Methods:** Conducted at the National Oncology Teaching Hospital in Najaf Governorate from September 2023 to March 2024, the study included 90 breast cancer patients and 90 controls. Serum levels of CA15-3, CEA, and Vitamin D3 were measured using ELISA, with statistical analysis performed using SPSS version 25. **Results:** The study found significant negative correlations between Vitamin D3 levels and the biomarkers CEA ($r = -.422, p = .001$) and CA15-3 ($r = -.499, p = .001$). Breast cancer patients had significantly lower Vitamin D3 levels (9.22 ± 0.07 ng/mL) than controls (35.62 ± 0.02 ng/mL, $p = .0001$). CA15-3 and CEA levels were significantly higher in patients compared to controls. **Implications** The findings suggest that Vitamin D3 may regulate tumor markers, impacting breast cancer outcomes and therapy. This supports the potential use of Vitamin D3 supplementation in breast cancer treatment.

Conclusion: our study indicated that the level of Vitamin D3 was inversely related to both CEA and CA15-3 whereby a high level of Vitamin D3 corresponded to the low level of these tumor markers This investigation highlights the need to ensure required Vitamin D3 levels in these patients with breast cancer and indicates that administration of Vitamin D3 could be a promising intervention strategy in the management of the Breast Cancer.

Keywords: Vitamin D3, Breast Cancer, CA15-3, CEA, Tumor Markers.

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INTRODUCTION

Breast cancer remains one of the leading diseases affecting women and is defined as the growth of malignant cells in the breast. Being one of the most prevalent malignancies in the world, it ranks high on the list of cancer deaths in women. Breast cancer is heterogeneous with regards to its subtype and origin, and the cause, which is genetic, environmental, and lifestyle-based, is complex (Bray et al., 2018).

The studies performed over recent years have been directed on the investigation of new potential biomarkers for breast cancer diagnosis at early stages, prognosis of the disease, and evaluation of the outcomes of the therapy. Among such biomarkers CEA and CA15-3 have

been examined profoundly in detail due to its stability in the circus. CEA is a tumor marker expressed in colorectal cancer where it is widely used in diagnosis as well as for monitoring patients but is also elevated in breast cancer, mainly in metastatic and recurrent types (Anoop

et al., 2022). CA15-3 is a Mucin glycoprotein that is secreted in to bloodstream by MUC- 1 gene which is over expressed in breast cancer and is used as a prognostic marker for evaluating progress of the disease and the effectiveness of treatment(Fu & Li, 2016). Also, Vitamin D3 is deemed important and has received focus since it can have protective effects against cancer. This oncoprotein is involved in cell proliferation, cell death, and the process of differentiation, and its scarcity has been linked with the increased density of breast cancer and poor survival rates(Feldman et al., 2016).

Therefore, while the studies examined here have noted some important progress, there are still considerable gaps to be filled, especially regarding the precise and specific correlation between Vitamin D3 and tumor markers such as CEA and CA15-3 in breast cancer patients. Several cross-sectional surveys have pointed towards a negative correlation of Vitamin D3 levels with mentioned biomarkers, indicating the role of Vitamin D3 in regulating tumor activity and hence its direct impact on cancer prognosis. However, there is a lack of systematic and empirical examination of these associations in the current literature, thus signifying the absence of existing research in this field (Abdullah et al., 2022; Mohr et al., 2011).

The present research could therefore be beneficial in filling this gap by analyzing the relationship between Vitamin D3 and the tumor markers CEA And CA15-3 in the BC patients. The goals include exploring the levels of CEA and CA15-3 in the blood plasma of breast cancer patients and determining whether there is a correlation between Vitamin D3 and these indicators; comparing the possibilities of using Vitamin D3 as a regulator of the specified tumor markers; and identifying the role of Vitamin D3 levels in predicting the outcomes of breast cancer interventions. The significance of this research relies on the fact that it is a holistic study since it aims at determining how the

nutrient Vitamin D3 influences basic markers of tumor; this would be instrumental in aiding in prognosis as well as treatment in breast cancer(Hossain et al., 2019).

METHODS

Study Design:This research adopts a case-control study design aimed at evaluating the association between Vitamin D3 levels and the tumor markers CEA and CA15-3 in breast cancer patients. The study was conducted at the National Oncology Teaching Hospital in Najaf Governorate from September 2023 to March 2024. The design is suitable for answering the posed research question, as it allows for a clear comparison between breast cancer patients and healthy controls.

Sample Population:The subjects in the present study included 90 female, adult breast cancer patients and 90 female, healthy individuals. All patients were confirmed or highly suspected to have breast cancer by specialized physicians and the data comprised patients who had newly diagnosed breast cancer before chemotherapy or during chemotherapy or hormone therapy. The participants were from 30 to 60 years of age. The control group was more a group of healthy females, distributed by the age and living area, similar to the patient group. **Data Collection Techniques and Instrument Development:**Approximately, five milliliters of blood was drawn from each participant, and the area of venipuncture was first cleaned with 70% alcohol and 2% iodine. Blood samples were taken in a gel tube for serological analysis. Serum samples were obtained by centrifugation of the blood samples at 3500 rpm for 15 minutes after which they were aliquoted and frozen at -20°C. Concentrations of CA15-3, CEA, and Vitamin D3 in serum and determined by Enzyme Linked Immunosorbent Assay(ELISA) method.

Data Analysis Techniques

Data were analysed using SPSS software version 25. More particularly, a comparison between patients and controls regarding the mean levels of CEA, CA15-3 and Vitamin D3 was performed by using ANOVA. Pearson’s correlation coefficients were applied to the variables of Vitamin D3 against the tumor markers with the significance level held at $p < 0.05$.

Sampling and Procedures: The sampling of the study involved various patients battling with breast cancer and the control group as well. Namely, procedures were subdivided into systematically ordered sub-steps, as well as specific titles of methods with clear descriptions of the alterations, for example new ELISA protocols. Demographics of the patients the data captured involved their age, gender and weight while other data captured was the serum level of biomarkers. Laboratory equipment and reagents like centrifuges and ELISA kits were mentioned in students’ explanations to justify accurate measurements.

RESULTS

The study aimed to evaluate the association between Vitamin D3 levels and the tumor markers CEA and CA15-3 in breast cancer patients. The data revealed significant findings that elucidate the potential modulatory role of Vitamin D3 in breast cancer. The mean levels of CEA and CA15-3 were significantly higher in breast cancer patients compared to the control group. Specifically, the mean CEA level in patients was 4.02 ± 1.12 ng/mL, whereas in

controls it was 1.96 ± 0.86 ng/mL ($p = 0.0001$). Similarly, the mean CA15-3 level in patients was 48.51 ± 13.7 U/mL, compared to 4.81 ± 1.91 U/mL in controls ($p = 0.0001$). Serum vitamin D3 concentration was observed to be relatively lower in the breast cancer patients as compared to the healthy control subjects. The mean of Vitamin D3 indices in patients was equal to 9.22 ± 0.07 . The median number of colonies was 07 ng/mL in the group with type 2 diabetes compared with 35 in the control group. 62 ± 0.02 ng/mL ($P = 0.0001$). The trend analysis that was performed using Pearson’s correlation coefficient gave a negative correlation between Vitamin D3 and CEA levels where the coefficient value was -0.422 and the P-value was less than 0.05 at 0.001. Also, a direct relationship was noted for Vitamin D3 with the tumour markers CA15-3, as regression analysis gave a negative correlation coefficient of -0.499 with a probability value of less than 0.001. Based on these findings it could be assumed that Vitamine D3 has an impact on tumor activity and cancer prognosis since patients with lower Vitamin D3 levels had higher levels of the described tumor markers. Thus, Vitamin D3 seems to be confident for playing a role of a modulator of tumor markers levels in breast cancer, as established by the negative and statistically significant strong correlations with Vitamin D3 levels of the both tumor markers, CEA and CA 15-3. These findings are important to note when it comes to the management of breast cancer; for this is an implication that Vitamin D3 supplementation could be helpful.

Table 1. Association CEA , CA15-3 with Vitamin D3 in Breast Cancer Patients.

CEA (ng/mL)	CA15-3 (U/mL)	Vitamin D3 (ng/mL)
4.02 ± 1.12	48.51 ± 13.7	9.22 ± 0.07
1.96 ± 0.86	4.81 ± 1.91	35.62 ± 0.02
$r = -0.422, p = 0.001$	$r = -0.499, p = 0.001$	

A negative correlation was evident between Vitamin D3 and CEA. The correlation coefficient -0.422 ; $P(0.001)$. Likewise, it was also found that Vitamin D3 and CA15-3 had a very mild negative relationship, where Vitamin D3 as the independent variable, the observed correlation coefficient was $r = -0.499$ at $p = 0.001$. From these findings, it can be inferred that patients with low Vitamin D3 are more likely to have higher quantities of these tumor markers, hence having a possibility of Vitamin D3 in modifying the tumor's behaviour and thereby the outcome of cancer. More negative correlations occurring between Vitamin D3 status and the CEA and CA15-3 indicate that Vitamin D3 can act as a controlling factor for tumor markers in patients with breast cancer. With these conclusions, it is noteworthy to take into account Vitamin D3 levels in the diagnosis and the treatment of breast cancer and further express the demand for the improvement of Vitamin D3 levels in the course of the disease.

DISCUSSION

CEA with Vitamin D3

Carcinoembryonic Antigen (CEA) is perhaps one of the most well-known tumor markers utilized in BC surveillance and treatment. From these research findings, it can be concluded that CEA levels are elevated in breast cancer patients as compared to healthy women. Moreover, compared to the controls, the mean CEA level in breast cancer patients was 4.02 ± 1 . In ADHD patients, A cuts off at 12 ng/mL while in the control group, at 1 ng/mL . $96 \pm 0.86 \text{ ng/mL}$ ($t = 4.184$; $p = .0001$). This became a very significant difference thereby justifying the use of CEA biomarker for breast cancer. (He et al., 2016). In addition, it was established that there was an inverse relationship between Vitamin D3 and CEA levels with a coefficient (r) of -0.422 and probability (p) of $.001$. The above analysis leads us to conclude that, there is a negative relationship between Vitamin D3 and CEA in

breast cancer patients implying that as Vitamin D3 levels decrease, the CEA levels increase. Vitamin D3, usually attributed to the regulation of calcium levels in the body and bone metabolism, is also important to cancer's cause and development. They also observed that its deficiency augments the risk of cancer and a poor prognosis. Possibly, Vitamin D3 plays potential roles in the alteration of growth, differentiation, and death of tumor cells. The negative sign that was found in this study implies that probably Vitamin D3 can act in a negative way on CEA levels that will affect tumor growth and progression. This is in agreement with past findings that pointed out that Vitamin D3 influences the mechanisms of the immune system and combating inflammation which plays an essential role in cancer formation and spread. (Feldman et al., 2016).

CA15-3 with Vitamin D3

The study established a negative relationship between Vitamin D3 and CA15-3 among breast cancer patients ($r = -.499$, $p = 0.001$) and this shows that Vitamin D3 level increases as CA15-3 level decreases. Another nutrient that has been assigned to the regulation of calcium content in the body and maintaining bone health is Vitamin D3; this nutrient has been associated with cancer prevention and progression where consumption of Vitamin D3 is deficient has been associated with high risks for cancer and poor prognosis. In relation to the above-stated objectives, estramustine may affect tumor biology through control of cell proliferation, differentiation, and apoptosis influenced by Vitamin D3. The negative association stated implies that sufficient levels of Vitamin D3 could help decrease levels of CA15-3, influencing tumor development and progression. This is in agreement with other studies that have postulated that Vitamin D3 has effects on directing immune responses and

decreasing inflammation which are major aspects of carcinogenesis and metastatic processes. The study noted that the breast cancer patients had considerably low levels of Vitamin D3 as compared to the control group ($p < .0001$) where the former had 9.22 ± 0.07 ng/mL whereas the latter had 35.62 ± 0.02 ng/mL. It was concluded that Vitamin D3 is inversely related to breast cancer. This disparity provides evidence for the postulation that Vitamin D3 deficiency is inflammatory and contributes to breast cancer incidence, aggression, and prognosis; owing to Vitamin D's involvement in cellular functions such as growth, aging, and death. (Fu & Li, 2016; Hussien et al., 2021).

CONCLUSION

This paper aimed at establishing the relationship between Vitamin D3 and the biomarkers, CEA and CA15-3 on breast cancer clients. When comparing the patient's group to the control, the results showed that breast cancer patients had significantly elevated serum CEA and CA15-3 concentrations. Moreover, the mean level of Vitamin D3 was inversely related with both CEA and CA15-3 whereby high level of Vitamin D3 corresponded to the low level of these tumor markers. Hypothesized, these results indicate how Vitamin D3 could help control and perhaps affect the course of breast cancer by regulating tumor markers. Therefore, the current research adds its voice to the existing body of scientific research since it found indication that Vitamin D3 may be useful in the treatment of breast cancer. However, care must

be taken when generalizing the findings since the sample, and setting used in this study may not be representative of the entire population. Consequently, from the findings of the present study, the future research should work towards establishing the possible therapeutic role of Vitamin D3 supplementation among the breast cancer patients. But as a start, further research should be conducted with a higher number of patients and more diverse origin to see the observed correlations and to investigate the pathways of Vitamin D3 effects on tumor markers and carcinogenesis. Moreover, meta-analyses for this topic should be conducted on specifically investigating the data for a longer term that indicates the significant impacts of Vitamin D3 supplementation on the prognosis of BC. Further studies focusing on using Vitamin D3 alongside with other treatments will enable researchers to establish whether the vitamin can be of any additional benefit in managing breast cancer. Thus, this investigation highlights the need to ensure required Vitamin D3 levels in these patients with breast cancer and indicates that administration of Vitamin D3 could be a promising intervention strategy in the management of the disease.

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