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Association between serum vitamin A levels and molecular tumor subtypes in breast cancer patients undergoing radiotherapy

Associação entre níveis séricos de vitamina A e subtipos moleculares tumorais em pacientes com câncer de mama em radioterapia

Asociación entre niveles séricos de vitamina A y subtipos moleculares tumorales en pacientes con cáncer de mama en radioterapia

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ABSTRACT

Objective: To evaluate the association between serum vitamin A levels and tumor characteristics in patients with breast cancer undergoing radiotherapy, focusing on hormone receptor status and the triple-negative subtype. **Methods:** Prospective cohort study conducted between February and June 2025 including 50 women with breast cancer who underwent primary surgery and were referred for radiotherapy at an oncology center in Rio de Janeiro, Brazil. Clinical and lifestyle data were collected. Serum vitamin A levels were measured by high-performance liquid chromatography before radiotherapy. Deficiency was defined as <0.30 mg/L. Statistical analyses included t-tests, chi-square or Fisher's exact tests, and relative risk (α=5%). **Results:** Mean age was 54.6 ± 12.2 years; 26% had vitamin A deficiency. ER-positive and PR-positive tumors showed higher levels than negative tumors. Triple-negative breast cancer showed the lowest mean levels and highest deficiency prevalence (RR=3.43). No associations were found with BMI, smoking, alcohol use, HER2 status, or prior chemotherapy. **Conclusion:** Vitamin A deficiency was associated with hormone receptor-negative tumors, particularly the triple-negative subtype.

Keywords: Vitamin A deficiency, Oxidative stress, Breast neoplasms, Radiotherapy, Vitamin A.

RESUMO

Objetivo: Avaliar a associação entre níveis séricos de vitamina A e características tumorais em pacientes com câncer de mama submetidas à radioterapia, com ênfase nos receptores hormonais e no subtipo triplo-

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negativo. **Métodos:** Estudo de coorte prospectivo realizado entre fevereiro e junho de 2025 com 50 mulheres com câncer de mama submetidas à cirurgia primária e encaminhadas à radioterapia em centro oncológico no Rio de Janeiro. Coletaram-se dados clínicos e de estilo de vida. A vitamina A sérica foi dosada por cromatografia líquida de alta eficiência antes da radioterapia. Definiu-se deficiência como <0,30 mg/L. Utilizaram-se testes t, qui-quadrado ou Fisher e risco relativo (α=5%). **Resultados:** A média de idade foi 54,6 ± 12,2 anos; 26% apresentaram deficiência de vitamina A. Tumores ER+ e PR+ apresentaram níveis mais elevados que os negativos. O subtipo triplo-negativo apresentou menores níveis médios e maior prevalência de deficiência (RR=3,43). Não houve associação com IMC, tabagismo, etilismo, HER2 ou quimioterapia prévia. **Conclusão:** A deficiência de vitamina A associou-se a tumores sem receptores hormonais, especialmente ao subtipo triplo-negativo.

Palavras-chave: Deficiência de vitamina A, Estresse oxidativo, Neoplasias da mama, Radioterapia, Vitamina A.

RESUMEN

Objetivo: Evaluar la asociación entre niveles séricos de vitamina A y características tumorales en pacientes con cáncer de mama sometidas a radioterapia, con énfasis en receptores hormonales y subtipo triple negativo. **Métodos:** Estudio de cohorte prospectivo (febrero–junio de 2025) con 50 mujeres con cáncer de mama sometidas a cirugía y remitidas a radioterapia en Río de Janeiro, Brasil. Se recolectaron datos clínicos y de estilo de vida. La vitamina A sérica se midió por cromatografía líquida de alta resolución antes de la radioterapia. La deficiencia se definió como <0,30 mg/L. Se aplicaron pruebas t, chi-cuadrado o Fisher y riesgo relativo (α=5%). **Resultados:** Edad media de 54,6 ± 12,2 años; 26% presentó deficiencia. Tumores ER+ y PR+ mostraron niveles más altos que los negativos. El subtipo triple negativo presentó menores niveles y mayor prevalencia de deficiencia (RR=3,43). No hubo asociación con IMC, tabaquismo, alcohol, HER2 ni quimioterapia previa. **Conclusión:** La deficiencia de vitamina A se asoció con tumores sin receptores hormonales, especialmente el subtipo triple negativo.

Palabras clave: Deficiencia de vitamina A, Estrés oxidativo, Neoplasias de la mama, Radioterapia, Vitamina A.

INTRODUCTION

In Brazil, breast cancer represents the most prevalent malignancy among women, excluding non-melanoma skin cancer, with significant impact on morbidity and mortality. According to national estimates, approximately 73,610 new cases are expected annually for the 2023–2025 period, corresponding to an incidence rate of 41.89 cases per 100,000 women, with higher prevalence in the South and Southeast regions (INSTITUTO NACIONAL DE CÂNCER, 2022; INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA, 2025).

Vitamin A is an essential micronutrient involved in multiple physiological processes, including cellular differentiation, immune regulation, and maintenance of epithelial integrity. Its biologically active forms, known as retinoids, exert their effects through nuclear receptors, modulating gene expression and influencing cellular proliferation and apoptosis, which are key mechanisms in cancer development (JIN Y, et al., 2022; KIM JA, et al., 2021).

Epidemiological studies have investigated the association between β-carotene and cancer risk, highlighting a possible protective role of this compound in different oncological contexts. In breast cancer, higher plasma concentrations of β-carotene have been associated with a reduced risk of estrogen receptor-positive tumors, suggesting a relevant interaction between carotenoids and hormonal pathways in breast carcinogenesis (TAKAHASHI N, et al., 2022).

Radiotherapy, in turn, is an essential therapeutic modality in the treatment of breast cancer, but it is associated with alterations in systemic antioxidant status. Evidence indicates that patients undergoing radiotherapy show a significant reduction in circulating levels of β-carotene, a phenomenon that tends to intensify as the tumor stage progresses. This finding suggests that dietary intake of β-carotene during treatment may contribute to maintaining redox balance, although this strategy should be interpreted with caution, considering the potential impact of antioxidants on therapeutic efficacy mediated by reactive oxygen species (WIELAND LS, et al., 2021; PERAITA-COSTA I, et al., 2022).

Retinoids, biologically active forms of vitamin A, have been extensively studied for their anticancer properties, mainly attributed to their ability to modulate gene expression through binding to specific nuclear receptors, such as retinoic acid receptors (RAR) and retinoid X receptors (RXR) (JIN Y, et al., 2022). These compounds play a key role in regulating cell differentiation, proliferation, and apoptosis, processes directly involved in tumor initiation and progression.

Retinol, the primary circulating form of vitamin A, is mainly derived from animal-based foods, while carotenoids, such as β-carotene, are obtained from plant-based sources and can be converted into retinol in the body. In addition to its classical role in vision physiology, vitamin A derivatives play essential roles in the growth and maintenance of epithelial and bone tissues, reinforcing their relevance in cell renewal processes and tissue integrity (ROSS et al., 2020). From a population perspective, socioeconomic factors play a determining role in vitamin A–related nutritional status. A higher prevalence of poverty is associated with reduced serum retinol concentrations, with inadequate dietary intake of fruits and vegetables being one of the main causes of this deficiency (HOLMES et al., 2021). This scenario may contribute to inequalities in exposure to potentially protective nutritional factors, impacting both the risk and clinical outcomes of breast cancer.

Building on these biological mechanisms, vitamin A has been increasingly associated with breast cancer development and progression, particularly through its role in regulating tumor cell differentiation, proliferation, and antioxidant homeostasis. In this context, retinoid signaling pathways may influence not only cellular behavior but also the tumor characteristics. Epidemiological evidence further supports this relationship, indicating that circulating levels of carotenoids, including β-carotene, may be associated with distinct tumor biological characteristics, especially hormone receptor status. These findings suggest that such compounds may contribute to the modulation of tumor phenotype and progression, potentially influencing disease behavior and clinical outcomes in breast cancer patients (PERAITA-COSTA I, et al., 2022; DEHNAVI MK, et al., 2024).

Furthermore, systematic reviews and meta-analyses have demonstrated that serum levels of vitamin A and its derivatives may be associated with breast cancer prognosis and survival outcomes. These findings support the hypothesis that vitamin A may act not only as a nutritional factor but also as a biological marker related to tumor behavior and progression (HE J, et al., 2018; FULAN H, et al., 2011).

Radiotherapy has also been shown to influence systemic antioxidant dynamics, contributing to alterations in circulating levels of compounds such as β-carotene and retinol. These changes may reflect an increased oxidative burden induced by ionizing radiation, which promotes the generation of reactive oxygen species (ROS) as a key mechanism of tumor cell damage. In this context, the reduction of endogenous antioxidants may represent both a consequence of treatment-related oxidative stress and a potential adaptive response of the organism. However, the modulation of antioxidant levels during radiotherapy remains a subject of ongoing debate, as exogenous supplementation could theoretically attenuate ROS-mediated cytotoxic effects on tumor cells, potentially impacting therapeutic efficacy. Thus, the balance between oxidative damage and antioxidant defense appears to be a critical factor in determining treatment outcomes (WIELAND LS, et al., 2021; LI Y, et al., 2021; HARRIS IS e DENICOLA GM, 2020).

Additionally, tumor molecular characteristics, particularly hormone receptor status and HER2 expression, play a central role in determining prognosis and therapeutic strategies in breast cancer. Emerging evidence suggests that these molecular subtypes may also be associated with differences in micronutrient metabolism, including vitamin A, although the underlying mechanisms remain incompletely understood (KIM JA, et al., 2021; LAVUDI K, et al., 2023).

Given the high incidence of breast cancer and the potential role of vitamin A in tumor biology, understanding the relationship between serum vitamin A levels and tumor characteristics may contribute to improved clinical and nutritional assessment of these patients. In this context, this study aims to evaluate the association between serum vitamin A levels and tumor characteristics in patients with breast cancer undergoing radiotherapy, with emphasis on hormone receptor status, the triple-negative subtype, body mass index, lifestyle factors, and prior chemotherapy exposure.

METHODS

This is a prospective cohort study conducted between February and June 2025 at a private radio-oncology center in southeastern Brazil, where patients are referred for radical radiotherapy as part of curative treatment for breast cancer.

A total of 50 patients were included, comprising all eligible women treated at the study center during the study period. Inclusion criteria were female patients aged ≥18 years, newly diagnosed with breast carcinoma, who had undergone primary surgery and were referred for radical radiotherapy.

Diagnosis was confirmed through clinical evaluation, imaging, and histopathological analysis. Patients with recent vitamin A supplementation, chronic liver or kidney disease, inflammatory or malabsorptive disorders, incomplete histopathological reports, or metastatic disease at diagnosis were excluded.

Data were collected using a structured form developed based on a literature review. Variables included sociodemographic characteristics (age and body mass index [BMI]), clinical history (previous chemotherapy, tobacco use, and alcohol consumption), tumor characteristics (estrogen receptor [ER], progesterone receptor [PR], HER2 status, and triple-negative breast cancer [TNBC]), and serum vitamin A levels (mg/L). Vitamin A deficiency was defined as serum levels <0.30 mg/L.

Clinical data were obtained from medical records and patient interviews. Blood samples were collected prior to radiotherapy initiation and analyzed using high-performance liquid chromatography (HPLC). Tumor biomarker data were obtained from histopathological reports.

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as absolute and relative frequencies. Body mass index was categorized according to World Health Organization criteria.

- Eutrophic: 18.5–24.9 kg/m²
- Overweight: 25.0–29.9 kg/m²
- Obesity: ≥30.0 kg/m²

Independent t-tests were used for comparison of means, while categorical variables were analyzed using chi-square or Fisher's exact tests. Relative risk (RR) was calculated for vitamin A deficiency across subgroups, with statistical significance set at $p<0.05$. Due to the limited sample size, multivariable regression analysis was not performed.

This study was approved by the Research Ethics Committee of the Fluminense Federal University, and all participants provided written informed consent prior to inclusion. Participants were informed about the study procedures through an information sheet. Confidentiality was maintained throughout, and all personal identifiers were removed during data analysis and reporting.

RESULTS

The mean age of participants was 54.6 ± 12.2 years. The mean serum vitamin A level was 0.39 ± 0.14 mg/L, and 13 participants (26%) were classified as vitamin A deficient (<0.30 mg/L), while 37 (74%) had sufficient levels (≥0.30 mg/L). The mean body mass index was 27.7 ± 4.5 kg/m² (**Table 1**).

Table 1 - Baseline Characteristics of Study Participants.

	Mean ± SD
Age (years)	54.6 ± 12.2
Vitamin A level (mg/L)	0.39 ± 0.14
Body Mass Index (kg/m²)	27.7 ± 4.5
Vitamin A status:	n (%)
Deficient (< 0.30 mg/L)	13 (26%)
Sufficient (≥ 0.30 mg/L)	37 (74%)

Source: Krumenauer KM, et al., 2026.

Estrogen receptor (ER) positivity was observed in 38 patients (76%), while 12 (24%) were ER-negative. Progesterone receptor (PR) positivity was identified in 34 patients (68%) and negativity in 16 (32%). HER2 positivity was observed in 8 patients (16%), and 42 (84%) were HER2-negative. Ten participants (20%) were classified as having triple-negative breast cancer (TNBC), whereas 40 (80%) were non-TNBC (**Table 2**).

Regarding nutritional status, 14 patients (28%) were eutrophic, 17 (34%) were overweight, and 19 (38%) were obese. Tobacco use was reported by 13 participants (26%), and alcohol consumption by 14 (28%). Previous chemotherapy was reported in 37 patients (74%) (**Table 2**).

Table 2 - Clinical, Molecular, and Lifestyle Characteristics of the Study Participants

ER Status	**n (%)**
negative	12 (24%)
positive	38 (76%)
PR Status	**n (%)**
negative	16 (32%)
positive	34 (68%)
HER2 Status	**n (%)**
negative	42 (84%)
positive	8 (16%)
Triple-Negative Breast Cancer (TNBC)	n (%)
No	40 (80%)
Yes	10 (20%)
BMI	**n (%)**
Eutrophic	14 (28%)
Overweight	17 (34%)
Obesity	19 (38%)
Tobacco use	**n (%)**
No	37 (74%)
Yes	13 (26%)
Alcohol consumption	**n (%)**
No	36 (72%)
Yes	14 (28%)
Previous chemotherapy	**n (%)**
No	13 (26%)
Yes	37 (74%)

Source: Krumenauer KM, et al., 2026.

Patients with estrogen receptor (ER)-positive tumors had higher mean vitamin A levels compared to ER-negative patients (0.42 vs 0.28 mg/L; p=0.002). Similarly, progesterone receptor (PR)-positive patients had higher levels compared to PR-negative patients (0.43 vs 0.31 mg/L; p=0.004). Patients with triple-negative breast cancer (TNBC) had lower vitamin A levels compared to non-TNBC patients (0.26 vs 0.42 mg/L; p=0.001).

No statistically significant differences were observed for HER2 status (p=0.516), body mass index (p=0.370), tobacco use (p=0.256), alcohol consumption (p=0.739), or previous chemotherapy (p=0.117) (**Table 3**).

Table 3 - Mean Vitamin A Levels (mg/L) According to Clinical, Molecular, and Lifestyle Variables.

	Mean vitamin A levels (mg/L)	statistical significance
ER Status		
Negative	0.28	0.002
Positive	0.42	
PR Status		
Negative	0.31	0.004
Positive	0.43	
HER2 Status		
Negative	0.40	0.516
Positive	0.36	
Triple-Negative Breast Cancer (TNBC)		
No	0.42	0.001
Yes	0.26	
BMI		
Eutrophic	0.41	0.370
Overweight	0.42	
Obesity	0.35	
Tobacco use		
No	0.40	0.256
Yes	0.35	
Alcohol consumption		
No	0.39	0.739
Yes	0.40	
Previous chemotherapy		
No	0.44	0.117
Yes	0.37	

Source: Krumenauer KM, et al., 2026.

Table 4 presents the distribution of vitamin A status (sufficient ≥ 0.30 mg/L and deficient < 0.30 mg/L) according to body mass index, lifestyle factors, prior chemotherapy, and tumor molecular characteristics.

Most eutrophic (78.6%), overweight (64.7%), and obese (79%) patients had sufficient vitamin A levels, with no statistically significant differences across BMI categories (p=0.551). Similarly, no significant associations were observed between vitamin A deficiency and tobacco use (p=0.234), alcohol consumption (p=0.329), or prior chemotherapy (p=0.780).

In contrast, statistically significant associations were identified between vitamin A deficiency and tumor receptor status. ER-negative patients showed a higher proportion of deficiency (50%) compared to ER-positive patients (18.4%) (p=0.03). Likewise, PR-negative patients presented higher deficiency rates (43.7%) compared to PR-positive patients (17.6%) (p=0.05).

The highest prevalence of deficiency was observed in patients with triple-negative breast cancer, in whom 60% were vitamin A deficient, compared to 17.5% among non-TNBC patients (p=0.006). No statistically significant association was observed between HER2 status and vitamin A levels (p=0.944).

Table 4 - Distribution of Vitamin A Status According to Clinical, Molecular, and Lifestyle Variables.

	Vitamin A Status (mg/L)		statistical significance
	Sufficient: ≥ 0.30 N (%)	**Deficient: < 0.30 N (%)**	
BMI			
Eutrophic	11 (78.6%)	3 (21.4%)	0.551
Overweight	11 (64.7%)	6 (35.3%)	
Obesity	15 (79%)	4 (21%)	
Tobacco use			
No	29 (78.4%)	8 (21.6%)	0.234
Yes	8 (61.5%)	5 (38.5%)	
Alcohol consumption			
No	28 (77.8%)	8 (22.2%)	0.329
Yes	9 (64.3%)	5 (35.7%)	
Previous chemotherapy			
No	10 (76.9%)	3 (23.1%)	0.780
Yes	27 (73%)	10 (27%)	
ER Status			
No	6 (50%)	6 (50%)	0.03
Yes	31 (81.6%)	7 (18.4%)	
PR Status			
No	9 (56.3%)	7 (43.7%)	0.05
Yes	28 (82.4%)	6 (17.6%)	
HER2 Status			
No	31 (73.8%)	11 (26.2%)	0.944
Yes	6 (75%)	2 (25%)	
Triple-Negative Breast Cancer (TNBC)			
No	33 (82.5%)	7 (17.5%)	0.006
Yes	4 (40%)	6 (60%)	

Source: Krumenauer KM, et al., 2026.

Table 5 presents the relative risk (RR) of vitamin A deficiency (<0.30 mg/L) according to nutritional, lifestyle, and tumor-related variables.

No relevant differences in risk were observed across BMI categories (RR=0.98). Similarly, tobacco use (RR=0.93) and alcohol consumption (RR=0.91) were not associated with increased risk of vitamin A deficiency. Previous chemotherapy also showed no association with increased risk (RR=0.76).

In contrast, significant associations were found in relation to tumor receptor status. ER-negative patients had a higher risk of vitamin A deficiency (50% vs 18.4%), with an RR of 2.71. Similarly, PR-negative patients showed increased risk (43.7% vs 17.6%), with an RR of 2.48.

The highest prevalence was observed in the triple-negative breast cancer group, in which 60% of patients were vitamin A deficient, compared to 17.5% among non-TNBC patients, resulting in an RR of 3.43.

No significant association was observed between HER2 status and vitamin A deficiency, with similar prevalence between HER2-positive and HER2-negative groups (RR=0.95).

Table 5 - Relative Risk Analysis.

	Vitamin A Status (mg/L)		RR
	Sufficient: ≥ 0.30 N (%)	**Deficient: < 0.30 N (%)**	
BMI			
Eutrophic	11 (78.6%)	3 (21.4%)	0.98
Overweight	11 (64.7%)	6 (35.3%)	
Obesity	15 (79%)	4 (21%)	
Tobacco use			
No	29 (78.4%)	8 (21.6%)	0.93
Yes	8 (61.5%)	5 (38.5%)	
Alcohol consumption			
No	28 (77.8%)	8 (22.2%)	0.91
Yes	9 (64.3%)	5 (35.7%)	
Previous chemotherapy			
No	10 (76.9%)	3 (23.1%)	0.76
Yes	27 (73%)	10 (27%)	
ER Status			
No	6 (50%)	6 (50%)	2.71
Yes	31 (81.6%)	7 (18.4%)	
PR Status			
No	9 (56.3%)	7 (43.7%)	2.48
Yes	28 (82.4%)	6 (17.6%)	
HER2 Status			
No	31 (73.8%)	11 (26.2%)	0.95
Yes	6 (75%)	2 (25%)	
Triple-Negative Breast Cancer (TNBC)			
No	33 (82.5%)	7 (17.5%)	3.43
Yes	4 (40%)	6 (60%)	

Source: Krumenauer KM, et al., 2026.

DISCUSSION

The present study demonstrated a significant association between serum vitamin A levels and specific molecular subtypes of breast cancer, particularly those lacking hormonal receptor expression. In contrast, no statistically significant associations were observed with clinical and lifestyle variables such as body mass index, smoking, alcohol consumption, and prior chemotherapy, reinforcing the hypothesis that tumor biology may play a more relevant role in determining vitamin A status than systemic factors (KIM JA, et al., 2021).

The prospective cohort design strengthens the internal validity of the findings, as data collection was performed prior to the initiation of radiotherapy, minimizing potential recall bias. Although the relatively small sample size represents a limitation, especially for subgroup analyses, the consistency of the observed associations supports the robustness of the results. Additionally, the exclusion of relevant confounding conditions, such as chronic inflammatory diseases and recent vitamin supplementation, suggests that the observed hypovitaminosis A reflects a true biological state at the time of assessment (HE J, et al., 2018).

Regarding tumor molecular characteristics, patients with estrogen receptor (ER)-positive and progesterone receptor (PR)-positive tumors presented higher serum vitamin A levels, whereas lower levels were observed in ER-negative and triple-negative breast cancer (TNBC) patients. These findings are consistent with previous studies indicating that vitamin deficiencies may be associated with specific molecular profiles of breast cancer and may influence tumor behavior and prognosis (DEHNAVI MK, et al., 2024; PERAITA-COSTA I, et al., 2022).

From a mechanistic perspective, the interaction between estrogen receptors and retinoic acid receptors (RAR) may partially explain these findings. Both receptor families share genomic binding sites and exert regulatory effects on genes involved in cellular proliferation and differentiation. This interaction has been previously described and may contribute to the dysregulation of retinoid signaling in ER-negative tumors, leading to reduced antiproliferative effects mediated by vitamin A (HUA S, et al., 2009; JIN Y, et al., 2022).

Furthermore, more aggressive phenotypes, such as TNBC, have been associated with increased expression of retinol transporters, including STRA6, which facilitates intracellular retinol uptake. This mechanism may contribute to a relative depletion of circulating vitamin A levels, reflecting increased metabolic demand by tumor cells. In this context, the association between lower serum vitamin A levels and TNBC observed in this study may reflect tumor-driven increased metabolic demand rather than inadequate nutritional intake alone (LAVUDI K, et al., 2023).

Epidemiological evidence further supports these findings, demonstrating that reduced serum levels of carotenoids and retinoids are associated with poorly differentiated tumors, higher recurrence rates, and worse clinical outcomes. These data reinforce the hypothesis that vitamin A may act as a biomarker of tumor aggressiveness and altered cellular differentiation pathways in breast cancer (ELIASSEN AH, et al., 2015; ROSA C, et al., 2023).

No significant association was observed between HER2 status and vitamin A levels, suggesting that HER2 signaling pathways may not be directly involved in retinoid metabolism. This finding is consistent with previous studies indicating that HER2 expression is more strongly associated with proliferative signaling pathways independent of micronutrient regulation (KIM JA, et al., 2021).

In contrast, clinical and lifestyle variables, including BMI, smoking, alcohol consumption, and prior chemotherapy, were not associated with vitamin A levels in this cohort. Although existing literature suggests that obesity and smoking may influence the metabolism of fat-soluble vitamins, these effects may have been attenuated due to the relatively small sample size or the homogeneity of the study population. Additionally, tumor-related metabolic alterations may exert a stronger influence on circulating vitamin levels than systemic lifestyle factors (HARRIS IS e DENICOLA GM, 2020).

Relative risk analysis reinforced these findings, demonstrating that ER-negative and PR-negative patients had a significantly higher likelihood of vitamin A deficiency, while TNBC patients showed the highest risk. These results support the hypothesis that vitamin A deficiency may be associated with more aggressive tumor phenotypes and may reflect increased oxidative stress and altered metabolic demands in these subtypes (LI Y, et al., 2021).

Despite these findings, this study has important limitations, including the small sample size, the single-center design, and the absence of detailed dietary intake assessment, which may limit the external validity of the results. Future studies with larger and more diverse populations, as well as longitudinal designs, are necessary to better elucidate the role of vitamin A in breast cancer biology and its potential clinical applications (DEHNAVI MK, et al., 2024).

CONCLUSION

This study demonstrated a significant association between vitamin A deficiency and specific molecular subtypes of breast cancer, particularly in estrogen receptor–negative, progesterone receptor–negative, and triple-negative tumors, which showed higher prevalence and relative risk of deficiency. No significant associations were observed with body mass index, alcohol consumption, tobacco use, or previous chemotherapy, indicating that vitamin A status is more closely related to tumor biological characteristics than to clinical or lifestyle factors. These findings suggest that serum vitamin A may act as a potential biomarker of tumor aggressiveness, especially in hormonally negative phenotypes. However, the limitations of this study, including the small sample size and single-center design, restrict the generalizability of the results. Therefore, further studies with larger and more diverse populations are necessary to confirm these associations and to better elucidate the role of vitamin A in breast cancer biology and its potential clinical applications.

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ETHICS APPROVAL

Approved by the Research Ethics Committee of the School of Medicine at Fluminense Federal University (CAAE 85130724.1.0000.5243).

DATA AVAILABILITY STATEMENT

The dataset generated and analyzed during this study contains sensitive clinical information. Due to ethical and confidentiality restrictions, the data are not publicly available. However, anonymized data may be provided by the corresponding author upon reasonable request for academic purposes.

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