AUIQ Technical Engineering Science

Manuscript 1047

Antioxidants and Metabolic Biomarkers: Clinical Insights in Breast Cancer Patients

Rania Kareem

Emad Yousif

Taghried Salman

Muna Bufaroosha

AUIQ TECHNICAL ENGINEERING SCIENCE 2025;2:97–103

ORIGINAL STUDY

Antioxidants and Metabolic Biomarkers: Clinical Insights in Breast Cancer Patients

Rania Kareem [a,b], **Emad Yousif** [a,*], **Taghried Salman** [a], **Muna Bufaroosha** [c]

[a] Department of Chemistry, College of Science, Al-Nahrain University, Baghdad, Iraq
[b] Department of Environmental Science, College of Energy and Environmental Sciences, Al-Karkh University of Science, Baghdad, Iraq
[c] Department of Chemistry, College of Science, United Arab Emirates University, Al-Ain, UAE

ABSTRACT

Breast cancer is the primary cause of cancer-related deaths among women and the most common life-threatening malignancy identified in this population. The second most common cause of cancer-related fatalities in women is breast cancer. According to the most recent Iraq Cancer Requisition, breast cancer is the most common kind of cancer in women in Iraq, making up almost one-third of all female malignancies. Total of 100 patients with breast cancer was used in this study and compared to 100 healthy groups. Serum levels of vitamin C, vitamin E, Triglycerides, HDL, prolactin, cysteine protease, glutathione peroxidase and glutathione reductase were measured by standard methods. The study reported that HDL, Triglycerides, glutathione reductase, glutathione peroxidase, cysteine protease and prolactin were significantly increased in patient with breast cancer, while vitamin E was not significantly increased in the same patients. In addition, vitamin C levels were significantly decreased ($p < 0.0001$) in patients group when compared with healthy controls.

Keywords: Triglycerides, Glutathione peroxidase, Cysteine protease, Glutathione reductase, Prolactin, Breast cancer, Parameters

1. Introduction

Breast cancer is the second most prevalent non-skin cancer type (after lung cancer) and the fifth most common cause of cancer-related deaths in women, accounting for 10.4% of all cancer occurrences [1]. About one-third of all cancer cases reported in Iraq in 2019 were breast cancer, making it the leading cause of death for Iraqi women [2]. According to the most recent Iraqi Cancer Registry, breast cancer accounts for almost one-third of all female malignancies reported in Iraq, making it the most frequent kind of cancer among women. This demonstrates that, among the Iraqi population as a whole, breast cancer is the most common cancer location, exceeding even bronchogenic cancer. The World Health Organization has said that the best chance of lowering the death rate from breast cancer is by early identification and screening, particularly when paired with appropriate treatment. This served as the foundation for the 2001 launch of the Iraqi national program for breast cancer early detection, which aimed to downstage the illness at the time of presentation. Since then, major hospitals in every province in Iraq have set up dedicated clinics and facilities for the early diagnosis of breast malignancies [3].

Humans need vitamin C because it functions as an antioxidant and a cofactor in a number of enzymatic processes. Dioxygenase enzymes are involved in these reactions and are involved in several physiological processes, including the production of collagen, carnitine, and norepinephrine. as well as histone demethylation, hypoxia-inducible transcription factor (HIF) modulation, and serotonin production [4, 5].

Received 2 September 2025; revised 17 September 2025; accepted 18 September 2025.
Available online 23 September 2025

* Corresponding author.
E-mail addresses: rania.pchs24@ced.nahrainuniv.edu.iq (R. Kareem), emad.yousif@nahrainuniv.edu.iq (E. Yousif), taghried.salman@nahrainuniv.edu.iq (T. Salman), muna.bufaroosha@uaeu.ac.ae (M. Bufaroosha).

https://doi.org/10.70645/3078-3437.1047

Since humans cannot produce vitamin C like the majority of other mammalian species do, it is a necessary dietary component that they must obtain from outside sources such fruits and vegetables [6]. Vitamin E is the most important lipophilic antioxidant in biological systems, serving as the first line of defense against unsaturated fatty acid peroxidation [7]. It has recently been determined that this vitamin helps slow the formation of malignant cells. Additionally, it has been demonstrated that vitamin E can suppress estrogen receptor-positive breast cancers by acting as an antioxidant [8]. Glutathione peroxidase (GPxs), which use glutathione (GSH) as a reductant to convert hydroperoxides to water and alcohols, are essential enzymes in cellular antioxidant defense. The presence of either cysteine or selenocysteine at the active regions distinguishes the eight isoforms (GPx1–8) of this enzyme family [9]. GPxs are direct antioxidant enzymes that shield cells from oxidative damage, which is crucial for preserving cellular homeostasis. Different GPx isoforms have been connected to patient survival and prognosis across a range of cancer types, demonstrating their importance in the field of cancer [10]. Glutathione reductase is a recognized factor that plays a crucial part in oxidative metabolism by way of the glutaredoxin system. Four, five GSH creates a reducing intracellular environment by converting the oxidized form of glutathione (GSSG) in live cells into reduced glutathione (GSH) [11]. There may be a basic role for GSH in regulating cellular function because of its significant influence on the activity of other redox-sensitive proteins and its ratio to its oxidized state [12]. It has been demonstrated that patients with gastrointestinal tract cancers have higher blood levels of oxidative stress markers, most likely as a result of the high levels of reactive oxygen species (ROS) produced. Serum samples from patients with gastric cancers showed elevated lipid peroxidation and notable variations in GSH levels and other pertinent enzyme activities, including glutathione peroxidase (GSHPx), glutathione S-transferase (GST), and GR, when compared to healthy blood donor controls. These findings demonstrated the presence of both oxidative stress and efficient defense mechanisms, which have been connected to GSH metabolism [13]. Triacylglycerol, another name for triglycerides, is the primary lipid component and source of stored energy in the body [14, 15]. According to studies, triglycerides are not only a component of metabolic syndrome but also directly reflect the state of fat metabolism, take part in the metabolic reprogramming of tumor cells, and are crucial in the occurrence, progression, and prognosis of breast cancer [15–18]. Studies have also demonstrated that metabolic syndrome is independently linked to breast cancer. Researchers have studied several facets of triglycerides and breast cancer because they are interested in the aberrations of triglycerides and how they relate to the onset and prognosis of breast cancer. Regrettably, these research have produced inconsistent outcomes [19]. In addition, high-density lipoproteins (HDL) can change the homeostasis of cancer cells by encouraging the elimination of cholesterol. The antioxidant, anti-inflammatory, anti-angiogenesis, anti-apoptotic, and immunomodulatory properties of HDL-associated apolipoproteins and enzymes can also have an overall anti-tumorigenesis impact [20]. A number of clinical studies have reported a significant correlation between serum HDL-C and cancer risk and outcomes, in addition to the abundance of in vitro and experimental evidence supporting HDLs' anti-cancer properties [21]. The biological mechanisms underlying these associations are still unknown. A correlation between lower HDL-C levels and certain cancer types, such as colorectal cancer (CRC), lung cancer (LC), breast cancer (BC), ovarian cancer (OC), thyroid cancer (ThC), and gastric cancer (GC), has been suggested by several observational studies [22]. The multipurpose pituitary hormone prolactin is essential for proper lobuloalveolar development, breastfeeding, and the proliferation and differentiation of healthy mammary epithelium. Prolactin is implicated in mammary carcinogenesis [23, 24], according to evidence from epidemiologic and laboratory investigations, with greater correlations for postmenopausal breast cancer, which improved risk prediction models [25]. A previous research in the Nurses' Health Study (NHS) and NHSII found that postmenopausal women, but not premenopausal women, had a higher risk of breast cancer if their plasma prolactin levels were higher than 11 ng/mL and assessed within 10 years of diagnosis. Prolactin levels assessed more than ten years before diagnosis did not correlate with risk [26, 27]. The cysteine residue in their active site identifies cysteine proteases, a category of proteolytic enzymes. The cytoplasm or lysosome contain the hepsins B, L, H, and S. Some cell types manufacture them under pathological conditions [28]. Both general processes like the degradation of intracellular proteins and more specialized ones like the selective activation of signaling molecules like interleukin, enkephalin, and protein kinase C or the breakdown of extracellular proteins like bone resorption and macrophage activity are mediated by cysteine proteases. Numerous investigations have connected the development of malignancies to the synthesis of intracellular cysteine proteases [29].

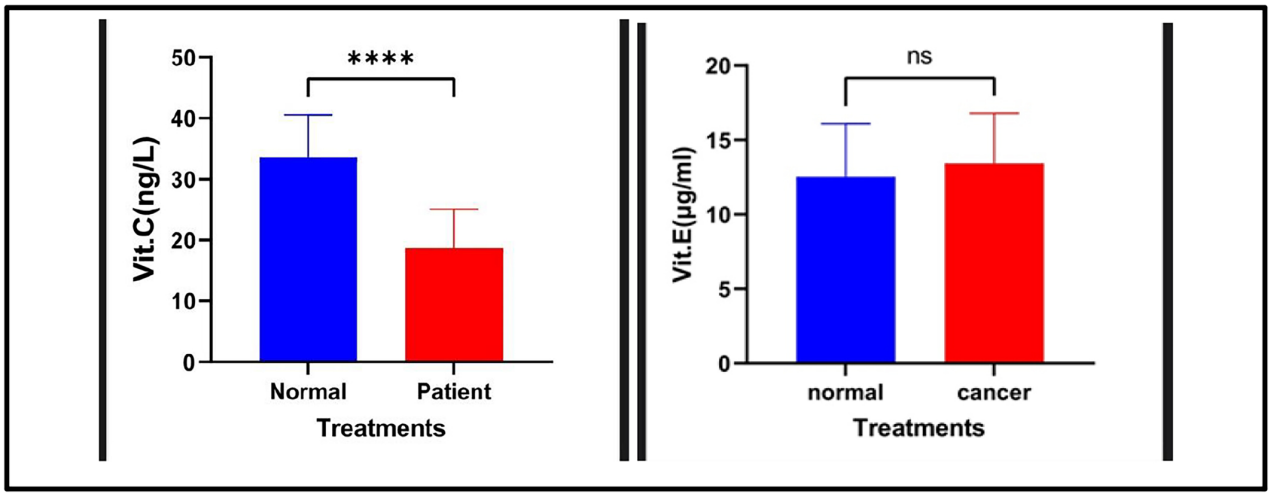

Fig. 1. The levels of vitamin C and vitamin E in serum of breast cancer patients.

2. Methodology

Study samples taken from Baghdadi patients with breast cancer that new diagnosed for age ranged between 20 to 65 years. The stage was different from stage 1 to stage 3 but all share in that they are new diagnosis before any treatment. Control groups were choosing also for healthy people not diagnosis in cancer before and age range it's the same 20 to 65 years. Five milliliters of blood were extracted from a patient's vein. Healthy controls were gathered from family members and friends. The gel tube was filled with venous blood. It was centrifuged for 10 minutes at 2500 rpm after clotting. For a subsequent test, the serum is transferred to Ependrof tubes and frozen at -20 ˚C. the biochemical parameters like vitamin C, vitamin E, glutathione peroxidase, glutathione reductase, HDL, Triglycerides, cysteine protease and prolactin were included in this study. The statistical analyses were done by pad graph prism t test including significant and SD.

3. Results and discussions

Results of this study appeared that there is a significantly ($P < 0.0001$) decreased in vitamin C level in serum of breast cancer patients but no significant($P=0.3956$) increase in vitamin E compared with control (Fig. 1). One of the leading causes of cancer death in women is breast cancer. Every year, it is the cause of the deaths of millions of women worldwide. It's a sickness. It often starts as a localized cell growth and eventually spreads to nearby lymph nodes before reaching the body's distal tissues (liver, lungs, bones, etc.). In the present study, it was observed breast cancer patients had decreased level in vitamin C, Because vitamin C has antioxidant properties that help lower free radicals, the growth and spread of tumors, and the vulnerability of cancer cells' blood vessels, which restricts vitamin C's ability to reach them, patients with cancer have lower vitamin C concentrations; High dosages of vitamin C have been found to help treat cancer patients because it promotes apoptosis by producing H2O2 from ascorbate oxidation, halting the S phase, reducing the growth of cancer cells, and influencing gene expression. Changes in cancer cells and vitamin C increase patient survival [30]. While, a no significant increasing in vitamin E was observed in the same patients. Several studies suggest that vitamin E may be a good option for cancer adjuvant treatment because of its anticarcinogenic properties. The discovery that people in the Mediterranean region, whose diets are high in different forms of vitamin E, show a lower risk of colon cancer than people in Northern Europe and the US, led to the first theory about the chemopreventive effects of vitamin E [31, 32]. By causing apoptosis and cell cycle arrest, vitamin E has an inhibitory impact on cell growth. There are two different ways that apoptosis happens: the intrinsic pathway, which is influenced by mitochondrial rupture that releases cytochrome c into the cytosol, and the extrinsic pathway, which is driven by death receptor signaling. Ultimately, these pathways come together to activate execution caspases, especially caspase-3, which causes poly-ADP-ribose polymerase (PARP) to fragment [33].

In addition, there is a significant increase in both glutathione peroxidase and glutathione reductase in serum of patients group (Fig. 2). One important component of the peroxyl scavenging process and the

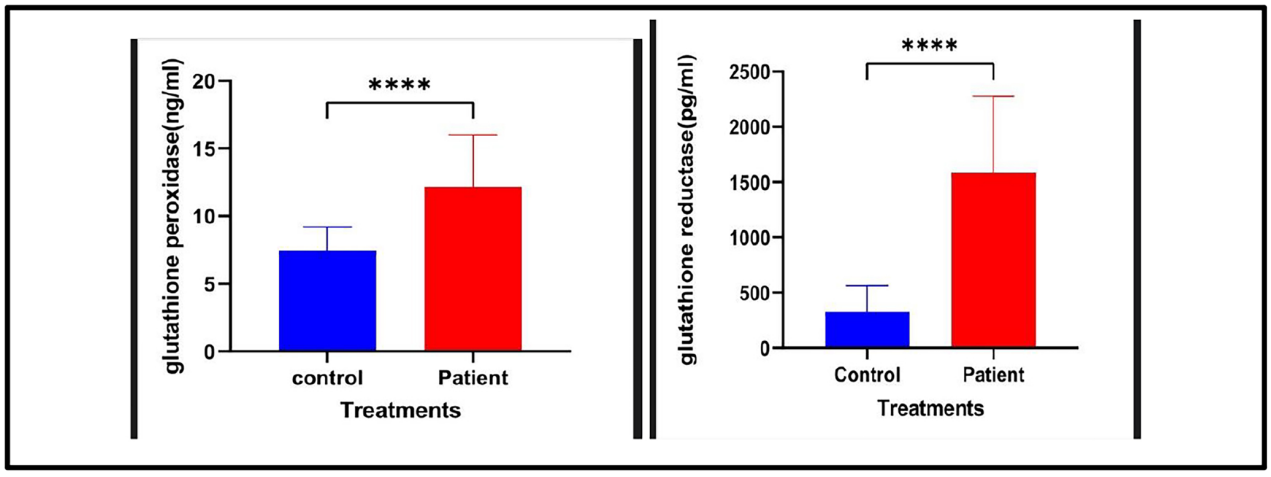

Fig. 2. The levels of glutathione peroxidase and glutathione reductase in serum of breast cancer patients.

preservation of the functional integrity of the cell membrane is glutathione peroxidase, an oxidative stress-inducible enzyme [34]. It has been proposed that elevated expression of genomic DNA may be the cause of the rise in glutathione peroxidase activity in breast cancer cell lines [35]. Moreover, GPx contributes significantly to carcinogenesis through modifications to the cyclooxygenase and lipoxygenase pathways [36, 37]. The increase in GPx activity may be the result of its activation to offset the effects of elevated oxidative stress. According to Skrydelwska [38], cancer tissue has elevated levels of glutathione reductase, glutathione peroxidase, and superoxide dismutase (SOD) along with a corresponding drop in Glutathione levels. They proposed that cancer cells' enhanced activity of these antioxidant enzymes would shield the cells from oxidative stress or damage. The higher use of Glutathion by antioxidant enzymes, which are combating the elevated oxidative stress brought on by ROS, may be the cause of the drop in Glutathione levels. Since glutathione reductase is necessary for Glutathione regeneration, decreased glutathione reductase activity may potentially contribute to Gluta depletion [39].

Also, the level of HDL and Triglycerides was measured and result shows there is a significant ($P < 000.1$) increasing in the level of these parameters (Fig. 3). The relationship between lipid profile and recurrence of breast cancer can be explained by a number of different processes. First, we may use dietary considerations to explain this outcome. The amount of food consumed has a direct impact on serum lipid levels, and dietary patterns can also have an impact on lipid profiles. A low-fat diet significantly decreased LDL levels, whereas a low-carb diet mostly affected Triglycerides and HDL levels, according to a study that examined the impact of dietary patterns on carbohydrate and fat content on blood lipid profiles in patients with breast cancer [40]. Furthermore, the serum lipid profile may serve as a proxy for nutritional status [41]. Remarkably little research has been done on how low dietary status affects breast cancer prognosis. The primary cause of this is the methodological challenges associated with implementing and sustaining lifestyle modifications in order to gather concrete proof of a causal association in a randomized controlled trial. Indirect evidence is supplied by observational studies using other indirect markers, such as BMI or lipid profile, which indicate the nutritional status, even though there is no evidence that dietary fat intake and blood lipid level affect the prognosis of breast cancer. An established risk factor and poor prognostic factor for breast cancer is obesity [42].

Finally, a significant ($P < 0.0001$) increasing in prolactin and cysteine protease levels was observed in the serum of patient groups in comparison with healthy groupn (control) as seen in Fig. 4. Cysteine proteases appear to be actively implicated in carcinogenesis based on their overexpression in serum. Numerous studies show that the cysteine proteases group's enzymes are important in a variety of carcinogenesis processes, and they are suggested as a possible target for cancer therapy [43]. The overexpression of cysteine proteases in cancer tissues, especially highly metastatic and invasive inflammatory breast cancer, has been shown in a number of investigations [44]. However, no correlation or an inverse link was noted in several research. Chen and Platt discovered that individuals with early-stage illness had greater levels of tissue cysteine proteases than those detected in late-stage tissues [45]. Accordingly, Kos et al.'s investigation revealed that the CatB/cystatin C complex, as measured by ELISA, was less prevalent in the sera

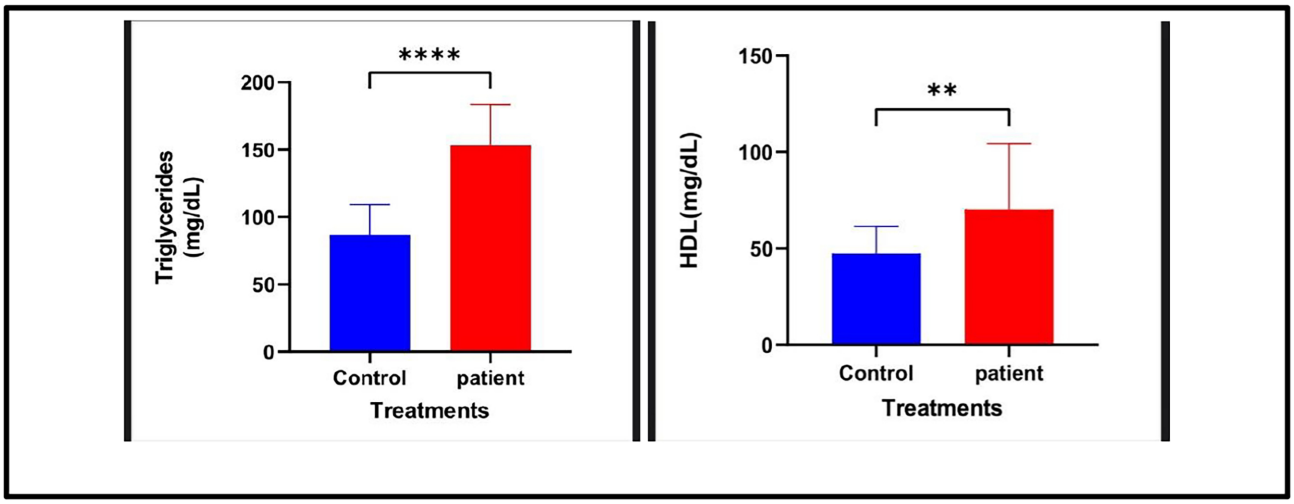

Fig. 3. The levels of Triglycerides and HDL in serum of breast cancer patients.

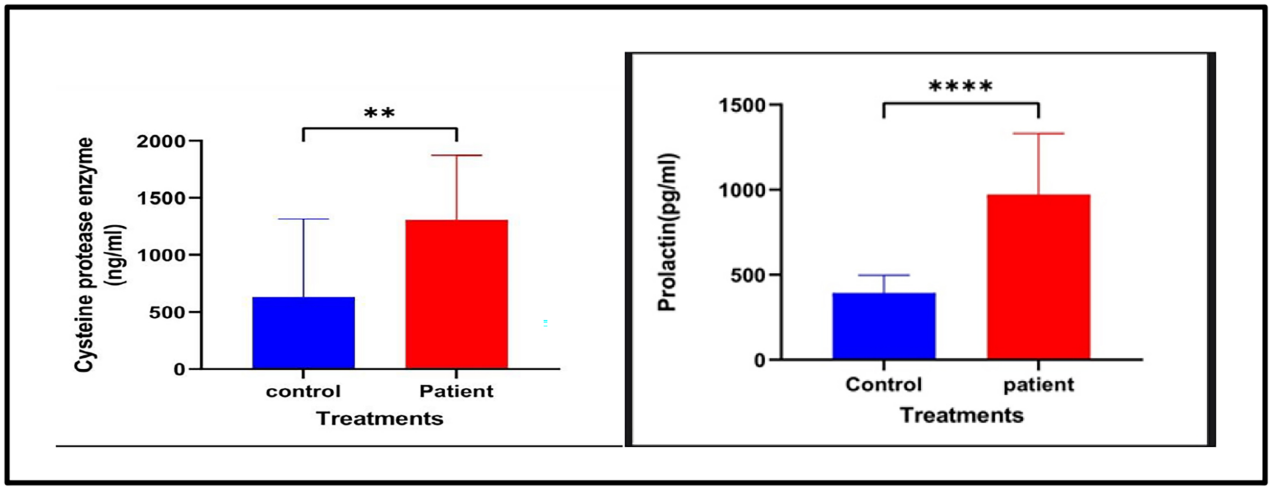

Fig. 4. The levels of cysteine protease and prolactin in serum of breast cancer patients.

of patients with malignant tumors compared to those with benign conditions and healthy controls [46].

Some studies conducted in the early 20s found a favorable correlation between the development of breast cancer and blood prolactin levels. But they were unable to identify a logical connection. In a thorough study published in 2003, Charles Clevenger et al. discussed the cellular, transgenic, and epidemiological aspects of prolactin's involvement in breast cancer They said that at least six distinct prolactin receptor isoforms allow prolactin to stimulate the proliferation of breast cancer cells at endocrine levels. Additionally, they stated that prolactin would work with other members of the cytokine receptor superfamily to activate certain signaling pathways. However, more recent studies on prolactin did not discover any such effects [47]. Nouhi evaluated the tumor suppression function of prolactin in breast cancer in a 2006 research that was published in the Cancer Research Journal. They found that epithelial-mesenchymal transition, which is essential for tumor metastasis, is regulated by prolactin and Janus-activated-kinase2. They said that the two primary prometastatic pathways, transforming growth factor-β/Smad and mitogen-activated protein kinase, were activated when PRL signaling was blocked. They ultimately came to the conclusion that prolactin most likely functions as a hormone that suppresses invasion in breast cancer [48, 49].

4. Conclusion

Breast cancer had a significant effect on all parameters (vitamin C, vitamin E, glutathione peroxidase, glutathione reductase, HDL, triglycerides, cysteine

protease and prolactin). All results were compared with samples from healthy individuals.

Acknowledgment

The authors gratefully acknowledge Al-Nahrain University for supporting this research.

Conflict of interest

The authors declare that there is no conflict of interest.

Data availability statement

All data will be available when request from the authors.

Author contributions

All authors have the same contributions

References

1. M. Jenifar, S. Sarathi, V. Hemavathy, and P. Balu, "Management of breast cancer: An overview," *Cardiometry*, 2023.
2. M. Y. Al-Hashimi, "Trends in breast cancer incidence in Iraq during the period 2000–2019," *Asian Pacific Journal of Cancer Prevention: APJCP*, vol. 22, no. 12, pp. 3889, 2021.
3. N. Aljubori, "Breast Cancer in Iraq," *International Journal of Medical Sciences*, vol. 1, no. 1, pp. 6–12, 2018.
4. J. Du, J. J. Cullen, and G. R. Buettner, "Ascorbic acid: Chemistry, biology and the treatment of cancer," *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer*, vol. 1826, pp. 443–457, 2012, doi: 10.1016/j.bbcan.2012.06.003.
5. P. Callen and M. M. Danik, "Vitamin C: Optimal dosages, supplementation and use in disease prevention," *Functional Foods in Health and Disease*, vol. 5, no. 3, pp. 89–107, 2015.
6. F. J. Roa, E. Pena, M. Gatica, and C. I. Rivas, "Therapeutic use of vitamin C in cancer: Physiological considerations," *Frontiers in Pharmacology*, vol. 11, pp. 211, 2020.
7. D. Larouche, M. Hanna, and S.-L. Chang, *et al.*, "Evaluation of antioxidant intakes in relation to inflammatory markers expression within the normal breast tissue of breast cancer patients," *Integrative Cancer Therapies*, vol. 16, pp. 485–495, 2017.
8. J. Donnely, A. Appathurai, H. Yeoh, D. Kate, and W. Faisal, "Vitamin E in cancer treatment: A review of clinical applications in randomized control trials," *Nutrients*, vol. 14, no. 20, pp. 4329, 2022.
9. P. Matoušková, B. Hanousková, and L. Skálová, "MicroRNAs as potential regulators of glutathione peroxidases expression and their role in obesity and related pathologies," *International Journal of Molecular Sciences*, vol. 19, p. 1199, 2018.
10. M. Paula, L. Carlos, L. Carlos, M. Michael, G. Jesus, and M. Javier, "Glutathione peroxidases: An emerging and promising therapeutic target for pancreatic cancer treatment," *Antioxidants*, vol. 13, no. 11, pp. 1405, 2024.
11. R. Siegel, D. Naishadham, and A. Jemal, "Cancer statistics, 2013," *CA: A Cancer Journal for Clinicians*, vol. 63, no. 1, pp. 11–30, 2013.
12. V. Stigliano, L. Sanchez-Mete, A. Martayan, and M. Anti, "Early-onset colorectal cancer: A sporadic or inherited disease?," *World Journal of Gastroenterology*, vol. 20, no. 35, pp. 12420–12430, 2014.
13. H. P. Ostendorff *et al.*, "Multiplexed VeraCode bead-based serological immunoassay for colorectal cancer," *Journal of Immunological Methods*, vol. 400–401, pp. 58–69, 2013.
14. Premenopausal Breast Cancer Collaborative Group, M. J. Schoemaker, and H. B. Nichols, *et al.*, "Association of body mass index and age with subsequent breast cancer risk in premenopausal women," *JAMA Oncology*, vol. 4, no. 11, pp. e181771, 2018.
15. I. J. Neeland, S. Lim, and A. Tchernof, *et al.*, "Metabolic syndrome," *Nature Reviews Disease Primers*, vol. 10, no. 1, pp. 77, 2024.
16. S. Dong, Z. Wang, K. Shen, and X. Chen, "Metabolic syndrome and breast cancer: Prevalence, treatment response, and prognosis," *Frontiers in Oncology*, vol. 11, pp. 629666, 2021.
17. Z. Gong, Q. Li, J. Shi, E. T. Liu, L. D. Shultz, and G. Ren, "Lipid-laden lung mesenchymal cells foster breast cancer metastasis via metabolic reprogramming of tumor cells and natural killer cells," *Cell Metabolism*, vol. 34, no. 12, pp. 1960–1976, 2022.
18. A. M. Mohammed, H. B. Hamed, M. K. Noaman, and N. Alieldin, "Metabolic syndrome and breast cancer risk," *Journal of the Egyptian National Cancer Institute*, vol. 35, no. 1, pp. 42, 2023.
19. W. Zhang, Z. Li, Y. Huang, J. Zhao, S. Guo, W. Qian, and G. Sihan, "Complex role of circulating triglycerides in breast cancer onset and survival: Insights from two-sample Mendelian randomization study," *Cancer Medicine*, vol. 14, no. 4, pp. e70698, 2025.
20. E. Morin, A. Xiang, and S. Anaa, "HDL in endocrine carcinomas: biomarker, drug carrier and potential therapeutic," *Frontiers in Endocrinology*, vol. 9, 2018.
21. G. Shiva, R. Biagio, P. Matteo, L. Stephen, M. Banach, and A. Sahebkar, "High-density lipoprotein components and functionality in cancer: State-of-the-art," *Trends in Endocrinology & Metabolism*, vol. 30, no. 1, pp. 12–24, 2019.
22. G. Shiva, R. Biagio, P. Matteo, L. Stephen, Z. Fras, and A. Sahebkar, "HDL and cancer – causality still needs to be confirmed? Update 2020," *Seminars in Cancer Biology*, vol. 73, pp. 169–177, 2021.
23. K. Tikk, D. Sookthai, T. Johnson, S. Rinaldi, I. Romieu, A. Tjonneland, A. Olsen, K. Overvad, F. Clavel-Chapelon, and L. Baglietto, *et al.*, "Circulating prolactin and breast cancer risk among pre- and postmenopausal women in the EPIC cohort," *Annals of Oncology*, vol. 25, no. 7, pp. 1422–1428, 2014.
24. S. S. Tworoger, A. H. Eliassen, X. Zhang, J. Qian, P. M. Sluss, B. A. Rosner, and S. E. Hankinson, "A 20-year prospective study of plasma prolactin as a risk marker of breast cancer development," Cancer Research, vol. 73, no. 15, pp. 4810–4819, 2013.
25. S. S. Tworoger, X. Zhang, A. H. Eliassen, J. Qian, G. A. Colditz, W. C. Willett, B. A. Rosner, P. Kraft, and S. E. Hankinson, "Inclusion of endogenous hormone levels in risk prediction models of postmenopausal breast cancer," *Journal of Clinical Oncology*, vol. 32, no. 28, pp. 3111–3117, 2014.
26. X. Zhang, M. Rice, S. S. Tworoger, B. A. Rosner, A. H. Eliassen, R. M. Tamimi, A. D. Joshi, S. Lindstrom, J. Qian, and G. A. Colditz, *et al.*, "Addition of a polygenic risk score, mammographic density, and endogenous hormones to existing breast cancer risk prediction models: a nested case-control study," *PLoS Med.*, vol. 15, no. 9, pp. e1002644, 2018.

27. M. Gabrielson, K. Ubhayasekera, B. Ek, M. Andersson Franko, M. Eriksson, K. Czene, J. Bergquist, and P. Hall, "Inclusion of plasma prolactin levels in current risk prediction models of premenopausal and postmenopausal breast cancer," *JNCI Cancer Spectr.*, vol. 2, no. 4, pp. pky055, 2018.
28. S. Verma, R. Dixit, and K. C. Pandey, "Cysteine proteases: modes of activation and future prospects as pharmacological targets," *Front. Pharmacol.*, vol. 7, pp. 107, 2016.
29. N. K. Karamanos, A. Theocharis, Z. Piperigkou, D. Manou, and A. Passi, "A guide to the composition and functions of the extracellular matrix," *FEBS J.*, vol. 288, pp. 6850–6912, 2021.
30. P. Gao, H. Zhang, R. Dinavahi, F. Li, Y. Xiang, and V. Raman, *et al.*, "HIF-dependent antitumorigenic effect of antioxidants in vivo," *Cancer Cell*, vol. 12, pp. 230–238, 2007.
31. A. K. Smolarek, J. Y. So, P. E. Thomas, H. J. Lee, S. Paul, and A. Dombrowski, *et al.*, "Dietary tocopherols inhibit cell proliferation, regulate expression of ERa, PPAR?, and Nrf2, and decrease serum inflammatory markers during the development of mammary hyperplasia," *Mol. Carcinog.*, vol. 52, pp. 514–525, 2013.
32. P. Meganathan and J.-Y. Fu, "Biological properties of tocotrienols: evidence in human studies," *Int. J. Mol. Sci.*, vol. 17, pp. 1682, 2016.
33. C. S. Yang, P. Luo, Z. Zeng, H. Wang, M. Malafa, and N. Suh, "Vitamin E and cancer prevention: Studies with different forms of tocopherols and tocotrienols," *Mol. Carcinog.*, vol. 3, no. 4, pp. 365–389, 2020.
34. R. Chandra, R. Aneja, C. Rewal, R. Konduri, K. Dass, and S. Agarwal, "An opium alkaloid – papaverine ameliorates ethanol induced hepatotoxicity: Diminution of oxidative stress," *Indian J. Clin. Biochem.*, vol. 15, no. 2, pp. 155–160, 2000.
35. E. M. Noor, A. H. Firas, J. Jamel, and M. Salam, "Evaluation of glutathione peroxidase and glutathione reductase enzymes in Iraqi patients with colorectal cancer," *Al-Nahrain Journal of Science*, vol. 27, no. 1, pp. 37–41, 2024.
36. K. Luke, J. K. Sandhu, E. H. Mary, and M. C. Culf, "Role of glutathione in cancer: From mechanism to therapies," *Biomolecules*, vol. 10, no. 10, pp. 1429, 2020.
37. K. Elena, "Glutathione-dependent pathway in cancer cells," *Int. J. Mol. Sci.*, vol. 25, no. 15, pp. 8423, 2024.
38. A. V. Reddy, L. K. Killampalli, P. Ravi, S. Naag, G. Sreenath, and S. Kumar, "Analysis of lipid profile in cancer patients, smokers and nonsmokers," *Dental Research Journal*, vol. 13, no. 6, pp. 494–499, 2016.
39. G. H. Faisal, S. M. Taha, M. I. Hamzah, and M. H. Shatha, "Serum lipid profile in Iraqi patients with breast cancer," *Fac Mol Baghdad*, vol. 57, no. 4, pp. 316–319, 2015.
40. H. J. Thompson, S. M. Sedlacek, D. Paul, P. Wolfe, J. N. McGinley, M. C. Playdon, E. A. Daeninck, S. N. Bartels, and M. R. Wisthoff, "Effect of dietary patterns differing in carbohydrate and fat content on blood lipid and glucose profiles based on weight-loss success of breast-cancer survivors," *Breast Cancer Res.*, vol. 14, pp. R1, 2012.
41. J. Wang and Z. Hong, "Low plasma total cholesterol concentration: a sensitive evaluation marker in hospitalized patients with nutritional deficiency malnutrition," *J. Food Nutr. Res.*, vol. 2, pp. 551–555, 2014.
42. D. S. Chan, A. R. Vieira, D. Aune, E. V. Bandera, D. C. Greenwood, A. McTiernan, D. Navarro Rosenblatt, I. Thune, R. Vieira, and T. Norat, "Body mass index and survival in women with breast cancer—systematic literature review and meta-analysis of 82 follow-up studies," *Ann. Oncol.*, vol. 25, pp. 1901–1914, 2014.
43. L. Kramer, D. Turk, and B. Turk, "The future of cysteine cathepsins in disease management," *Trends Pharmacol. Sci.*, vol. 38, pp. 873–898, 2017.
44. M. A. Nouh, M. M. Mohamed, M. El-Shinawi, M. A. Shaalan, D. Cavallo-Medved, H. M. Khaled, and B. F. Sloane, "Cathepsin B: A potential prognostic marker for inflammatory breast cancer," *J. Transl. Med.*, vol. 3, pp. 1, 2011.
45. Chen and M. O. Platt, "Multiplex zymography captures stage-specific activity profiles of cathepsins K, L, and S in human breast, lung, and cervical cancer," *J. Transl. Med.*, vol. 9, pp. 109, 2011.
46. J. Gora and L. Rafal, "Involvement of cysteine proteases in cancer," *Curr. Med. Chem.*, vol. 22, no. 8, pp. 944–957, 2014.
47. P. Lempidakim, Z. Stefanos, V. Michou, and P. Eskitzis, "Breast cancer and prolactin: A lifetime relationship," Acta Endocrinologica, vol. 3, pp. 349–355, 2024.
48. K. H. Jaafae, S. H. Hassan, and A. O. Salam, "Relationship of prolactin serum levels and breast cancer with hematological factors among cases in Kerbala Province, Iraq," *International Journal of Medical Research and Health Sciences*, vol. 7, no. 4, pp. 82–87, 2018.
49. M. Mahdis, Sh. Hossein, A. Majid, T. Kobra, and K. R. Shahin, "Evaluation of prolactin receptor in triple negative breast cancer by immunohistochemistry as a predictive factor: A descriptive analytic study," *Journal of Obstetrics, Gynecology and Cancer Research*, vol. 8, no. 1, pp. 29–34, 2023.