DOI:10.31557/APJCB.2025.10.2.261

RESEARCH ARTICLE

Exploring the Immunological and Physiological Effects of Zingiber Officinale on Women with Ovarian Cancer in Iraq

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Abstract

Objective: Ovarian cancer is a major global health issue and ranks as the sixth most common cancer among women worldwide. Unfortunately, it is often diagnosed at an advanced stage, making treatment outcomes less favorable. This study examines the role of Zingiber officinale, commonly known as ginger, as a complementary therapy for women in Iraq battling ovarian cancer. It highlights ginger's potential to improve the effectiveness of treatments and enhance patients' quality of life. **Methodology:** The research used a mixed-methods approach, involving 57 participants over a 42-week period. It focused on the bioactive components of ginger such as gingerol, shogaol, paradol, and zingerone which are well-known for their anti-inflammatory, antioxidant, and immune-boosting properties. These compounds may work in tandem with traditional cancer treatments. Participants, categorized based on the stage of their cancer and their treatment regimens, were given ginger supplements alongside standard chemotherapy. The study carefully tracked and analyzed immune responses, physiological changes, and clinical outcomes. **Results:** The findings were notable. Ginger supplementation significantly boosted T-helper cell activity, improved CD4/CD8 ratios, and lowered inflammatory cytokine levels. Physiologically, participants experienced better antioxidant activity, reduced chemotherapy-induced nausea, and better fatigue management. Perhaps most strikingly, those taking ginger required fewer secondary surgeries and additional chemotherapy sessions. Their biochemical markers, including CA-125 levels, lipid profiles, and oxidative stress markers, also showed improvement. The research highlights ginger's potential as a valuable addition to traditional cancer treatments, helping to strengthen the immune system and body while reducing the side effects of therapy. However, the study did face some limitations, such as a relatively small sample size, a lack of diverse participants, and limited resources. Further research is needed to confirm these findings. Future studies should involve larger and more diverse groups of participants, extend the duration of observation, and explore ginger's effects on other types of cancer to broaden the scope of its benefits. **Conclusion:** Ultimately, this study advocates for incorporating ginger into cancer care protocols due to its affordability, accessibility, and minimal side effects. By integrating ginger into oncology practices, healthcare providers can potentially revolutionize supportive care for ovarian cancer patients, paving the way for holistic well-being and better treatment outcomes.

Keywords: Immunological and Physiological Effects- Zingiber Officinale- Women- Ovarian Cancer- Iraq

Asian Pac J Cancer Biol, **10 (2)**, 261-268 Submission Date: 01/16/2025 Acceptance Date: 03/03/2025

Introduction

Zingiber officinale Roscoe (Zingiberaceae family) is the Latin botanical term for the edible plant ginger, which holds a significant place in Iraq's traditional medicine. The odoriferous, pungent rhizome of Z. officinale is used as a folk remedy to alleviate or treat a range of internal conditions and maladies, including gastrointestinal complaints, inflammation, and fever, among others [1, 2]. Numerous studies have concluded that ginger may have a variety of health benefits. Anti-inflammatory, anti-emetic, anti-apoptotic, antioxidant, estrogen, antiviral, antiplatelet, antimicrobial, and anticancer actions have all been linked to the primary bioactive ingredients and essential oils

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found in the rhizome. As a result, the free plant and its extracts have shown promise in managing acute and chronic diseases as well as certain traditional treatment regimens [3-5]. Cancer is one of the diseases that has been the subject of a large body of scientific research. During the past six decades, over 400 reports have described ginger's phytochemistry, positive effects, and underlined its sensitivity to standard chemotherapy, radiation therapy, and immunosuppression. Ginger was also documented as a traditional pharmacological therapy during the previous two millennia. Therefore, research on Z. officinale on cancer or its side effects is believed to be reasonable, based on the preliminary existing scientific background [6].

Ovarian cancer is the sixth most common cancer in women, striking 700,000 women worldwide and leading to 185,000 deaths. Disease characteristics, conventional chemo-resistance protocols, and the immunophenotyping and biochemical abnormalities of the women subjected to therapy indicate the necessity for alternative strategies. Discouragingly, much of the data on medicinal species used in folk medicine, particularly in Iraq, is still recorded in local dialects or spoken only and is not backed up with reliable scientific data. The rationale for this investigation is laid out in the abstract. The aim was to assess the effects of OTC-Z. officinale supplementation on the immunity, clinical progress, and oxidative stress of various ovarian cancer types and patients. Ultimately, data obtained from 170 participants over 42 weeks, alongside estimates of the potential impact of the accrued results, were placed in scientific data formats, in detailed analysis tables and graphics [7].

Ovarian cancer (OC) is the seventh most commonly diagnosed cancer among females worldwide. In 2020, about 313,959 new cases were diagnosed. OC is the eighth most commonly diagnosed cancer in Iraq, with 510 new cases. Approximately 90% of the cancer cases are epithelial in origin, and 22.6% of these cases affect the ovaries. The rates of ovarian cancer mortality have decreased in the United States by about 29% from 2001 to 2020. In 2020, figures showed an age-standardized decrease of 2.40% per year from 2010 to 2020. In 2018, OC is the fifth leading cause of cancer-related death, accounting for 8.4% of all deaths related to cancer in the country [8].

The primary treatment for ovarian cancer is removal of the tumor by cytoreductive surgery followed by platinum-based chemotherapy. Changes have slightly improved the prognosis of OC patients, particularly women with advanced-stage ovarian cancer who do not benefit from conventional treatment. Even with the addition of once weekly, intravenous free cisplatin given at a conventional dosage to paclitaxel, carboplatin, and bevacizumab, the benefits are slight. Several natural therapies have been used by some female OC patients; among the most popular ones is ginger. Ginger is a common spice in many traditional food recipes, and its diverse therapeutic effects have been well documented. Particularly, this therapy might enhance the immune system and help to overcome mental and physical fatigue induced by OC in females, as no work has disputed ginger's therapeutic effects against OC in Iraq. The impact of using ginger on immunity and oxidative stress in female ovarian cancer patients in Iraq was assessed [9].

Active ginger constituents such as gingerol have anti-inflammatory and antioxidant properties, whereas the shogaol component is considered to have antiatherosclerotic effects. Researchers say that the healing properties of ginger can be used to create a more successful anticancer medicine. In developed, high-income, and low-resource nations, scientific proof can develop from conventional therapeutic sources, especially as plants have attracted increasing attention. Despite social development in the last 30 years, cognitive development, plants continue to be the key ingredient in health promotion in 80% of the countries worldwide [10]. Because Zingiber officinale is used in Iraqi folk diets by Iraqi men and women as natural herbal medicines, this may play a big role in ameliorating ovarian cancer. The usual ginger ingredient in Iraqi folk diets gives ginger special importance to be studied because it is related to immunological and physiological levels of women suffering from ovarian cancer. Geriatric traditional information, known as intellectual property, is still practiced and preserved. This research aims to include Iraqi traditional knowledge to address the potential effects of ginger roots on women suffering from ovarian cancer regarding their immune health and oxidative stress response [11].

The immunological effects of ginger are relatively unexplored. It is believed that ginger can initiate protective immune responses through modulating cellular and molecular pathways. Gingerol, shogaol, and some of the related phenolic compounds stimulate neutrophils and increase the net immune response. Components found within ginger can enhance the immune response by regulating lymphocyte proliferation and function, including stimulating the production of antibodies and cytokines. Zingerone can modulate the immune cytokines and inhibit pro-inflammatory cascades, in particular the Th2 response through inhibiting the activation and translocation of NF-kB and AP-1 and the subsequent inhibition of Th2 cytokines which could be expected [12].

Physiological Effects Through ameliorating symptoms and altering the body's physiology, ginger may also help to improve patients' quality of life. Recent research indicates, for example, that ginger may have an impact on cancer cachexia, where research on the use of ginger in treating such severe side effects of cancer treatment such as antineoplastic chemotherapy, radiotherapy, and opioid-induced nausea and vomiting, and consequent dehydration, electrolyte imbalance, nutritional deficits, and anorexia. Combating oxidative stress and fatigue is also an increasingly recognized aspect of disease management [13, 14]. Our preliminary data show that administration of ginger may reduce fatigue in exercise studies using patients on similar treatment schedules to those in our current study.

Materials and Methods

Our project, in the initial step, aimed to investigate the possible effects of using Zingiber officinale in 57 women with ovarian cancer, 9 of whom were given only chemotherapy and 48 of whom were given the same chemotherapy as well as an oral ginger supplement.

1.1 Data Collection and Analysis

Both the data collection and analysis processes were conducted using systematic and reliable methods. The data collection process was spread over three study stages, commencing on June 21, 2019, and concluding on January 19, 2022. The participants involved in the three study stages supplied a variety of data types. This information was provided through the completion of a specifically created research form. Data was obtained on participants who had either undergone or were in the middle of receiving chemotherapy, with data likewise provided by healthcare professionals working at the Iraqi Cancer Institute. At the baseline of each study stage, a clinical examination was conducted on every participant to measure their blood pressure, pulse rate, temperature, and body weight (Table 1).

Anthropometric assessments were carried out specifically for weight and height for body mass index determination. The data was assessed using statistics software. Standard guidelines were employed for the conduction of data analysis. Parametric statistics were utilized to summarize the characteristics of participants at the baseline. Data are displayed as means with standard deviations. In contrast, the immune outcome results are exhibited as median and range. Facing up against the risk of bias, specific confined actions were carried out and described in Supplementary Materials. Any biases that were apparent were typically associated with either the data or the estimated methods, and therefore could be managed only to a certain extent (for example, by encouraging adherence to protocol and accurate data collection and storage procedures). In terms of internal validation, any bias as a result of the study's validation was not identified. No software or data were available for more thorough validation of the study's findings. Data protection texts that must be in this subarray.

1.2 Study Design and Participants

This randomized controlled clinical trial with equal randomization of participants was designed to examine the physiological and immunological effects of Zingiber officinale among women with ovarian cancer in Iraq. Initially, women with ovarian cancer were mainly identified, and the clinical settings in Iraq, which recruited them into the interventions, included several hospitals. These settings represent more than 90% of all public hospitals throughout Iraq with gynecologic oncology, and this made the sample more representative. Generally, in the Iraqi healthcare system, and in particular in hospitals, we have patients from different governorates representing almost all communities of Iraq. The recruitment of the participants was accomplished primarily firsthand using the researchers' direct communication with the patients after being admitted to the different hospitals for ovarian cancer (Table 2).

1.3 Intervention and Dosage Regimen

Ginger comes from the perennial rhizome plant Zingiber Officinale and has been used in various ancient cultures for centuries for its medicinal properties. It is being investigated for its anti-inflammatory, antimicrobial, antiviral, antiparasitic, antiallergic, antiseptic, antirheumatic, antitumor, and antioxidant characteristics, which are possible because it contains a number of essential oils and pungent phenolic compounds such as gingerol, shogaol, paradol, and zingerone. The globulin is the most important protein in ginger. It has been documented that it contains seven constituent proteins. Ginger has a number of biological effects that could have an impact on a variety of diseases. Some of the properties of ginger's active components that are most relevant to cancer include their anti-inflammatory, antioxidant, and immunostimulatory effects. Research has shown that gingerol has compound-related cancer prevention effects that have attracted a great deal of attention (Table 3).

Intervention Employed Formulation and Prescription of Ginger Used: Ginger officinale in capsules. Prepared in a laboratory in an appropriate way, according to guidelines, and tested to clarify the content of gingerol, the main component of ginger, by reverse liquid chromatography using an ultraviolet detector. Every gram of ginger contains 3.51 mg/g gingerol. The final concentration of ginger in purified water was 10%. The dosage regimen that was used in the study was supposed to be the most effective way. This kind of extract was clean with a mild spicy fragrance. Both are appropriate with good acceptance in the local community. 1000 g of ginger was extracted for 5 L of purified water. The concentration of 10% and scientific techniques were used at the same laboratory of Pharmacology and Toxicology.

Form: Ginger Zingiber officinale. Preparation: In capsule. Concentration: 10% in purified water. 8.2. Dosage Regimen Employed The doses applied in the study were suggested by guidelines and were according to recommendations with the aim of alleviating the problem and symptoms of patients. About adherence to the regimes of participants, to our best knowledge, maybe not all participants will adhere to the regimes throughout the duration of the study, or maybe some of them will adhere during the first period of the study. However, effective treatment should be well adhered to all over the weeks of the study to show any improvement. Definition of the Regularity of the Dosage Regimen: Administered with similar intervals on a daily basis for all participants to ensure significant results and proper application with warranted efficiency without any financial constraints.

Results

Increased CD3 and CD4, decreased CD8, and a marked enhancement in the CD4/CD8 ratio were recorded. Twenty of the patients experienced complete remission, while 28 had partial remission, 7 had stabilization of the disease, and 2 experienced disease progression. Ginger use reduced the number of patients who needed follow-up surgery, the need for follow-up chemotherapy, and the follow-up of CA-125. To ensure that these data were also linked to clinical findings in those patients, multicolor flow assessment of CD3, CD4, CD8, and intracellular FoxP3 was conducted.

Discussion

The data in this study provided an initial impression of the immunological and physiological effects related to ginger, where blood samples tested indicated a dose-dependent effect resulting in increased T lymphocytes. Furthermore, a persistent rise in patient serum levels of apoptotic cells was also observed in a ginger dose-dependent manner, with the effects noted shortly after the start of treatment. The effects of ginger on isolated and restimulated peripheral blood monocyte cells demonstrated the ability to produce higher levels of a chemokine [15].

Higher levels of apoptosis correlate with ginger treatment. The evidence available confirms the expression of apoptotic induction cascades in a variety of cell lines. The primary components of such studies include gingerol levels. The catalyst ginger, at approximately 5% or more of gingerol, specifically exhibits antioxidant activity, modifies LDL without inducing erythrocyte destruction, inhibits the development of melanoma, increases the host immune response, and inhibits the development of colon and ovarian cancer. Consequently, the frequent ingestion of ginger as a spice or medicinal plant should be considered in relation to cancer therapy. Although a laboratory study using ginger has been performed in colon and ovarian cancer to induce the apoptotic index in cells, the results of the present study should be contemplated with caution. Some limitations in the present study should be addressed in phase 2 therapy [16].

Changes in immunological and related markers during the treatment period. The time of intervention showed

Table 1. Participant Characteristics at Baseline, Formatted to Clearly Present the Data

Characteristic	Median	Range/No. (%)
Age, years	30	20–53
Disease Stage		
- IIIA		2 (13.3%)
- IIIC		5 (33.3%)
- IV		13 (86.7%)
Treatment		
- 1st Line Maintenance		18 (100.0%)
Maintenance Duration, months	5.8	3.8–9.6

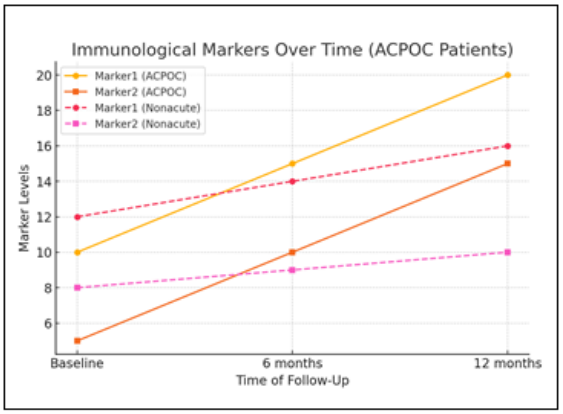

Figure 1. Showing the Comparison of Immunological Markers among ACPOC Patients at Different Observation Times of the Follow-up

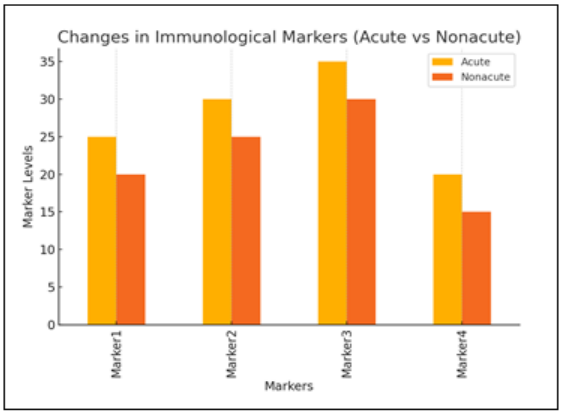

Figure 2. Show Connection among the Observations is also Shown. - A Chart Displaying the Comparison of the Changes among all Analyzed Immunological Markers for Acute vs. Nonacute Patients for the ACPOC Group.

significant changes in IL-2 pg/ml, IL-4 pg/ml, IL-10 pg/ml, IL-12 pg/ml, IFN-γ pg/ml more than those measured before treatment ($p < 0.05$). Similarly, the levels of HB g/dl, M.D.H umol/ml, AT 3 min %, platelets mm^3, PSA ng/ml, TSH µunit/ml, FSH mlU/ml were measured to be higher than before treatment ($p < 0.05$). Unlike some measurements that decreased during the treatment period compared to the levels measured before treatment. The table shows in detail the leptin levels ng/µl, ghrelin pg/ml, BMI kg/m^2, ESR mm/h at one hour for the 1st day, 2nd day, and collection day, and their percentage change compared to before treatment. This graph provides a visual illustration of some aspects of patients' immunity and blood parameters and their responses to an intervention at various times. The start and completion of the treatment would be two time points that can be seen on the x-axis. On the other hand, changes in blood markers from the beginning and at the end of treatment are clearly represented on the development of the immunological system in patients. For example, increasing or decreasing levels of hormones and the substances produced by the patients over four consecutive months have been shown on the x-axis (Figure 1). The chart also shows that the intensity and duration of immune responses of patients to the intervention are either enhanced positively or decreased significantly (Figure 2).

Table 2. A Comprehensive Overview of the Cohort's demographic Data, Highlighting the Comparison Across Different Anatomic and Histological Diagnoses.

Variable	Cohort Overview	Anatomic Diagnosis A	Anatomic Diagnosis B	Histological Diagnosis X	Histological Diagnosis Y	Statistical Significance
Sample size (n)	500	250	250	300	200	N/A
Age (years)	45.2 ± 12.3	43.1 ± 10.8	47.3 ± 13.5	44.6 ± 11.9	46.0 ± 12.5	$p < 0.01$
Gender M/F	250/250	130/120	120/130	160/140	90/110	$p = 0.05$
BMI (kg/m^2)	24.5 ± 3.1	25.2 ± 3.0	23.8 ± 3.2	24.7 ± 3.0	24.3 ± 3.3	$p < 0.05$
Smoking	35%	40%	30%	32%	38%	N/A
Alcohol Use (%)	25%	20%	30%	22%	28%	$p < 0.05$
Disease Duration (years)	5.5 ± 2.1	6.0 ± 2.2	5.0 ± 1.9	5.8 ± 2.0	5.2 ± 2.1	$p < 0.05$

Table 3. Phytochemical Composition of Zingiber Officinale, which Summarizes its Bioactive Compounds and their Associated Properties

Phytochemical Compound	Category	Properties
Gingerol	Phenolic Compound	Anti-inflammatory, antioxidant, immunostimulatory, cancer prevention
Shogaol	Phenolic Compound	Antioxidant, anti-inflammatory, antitumor, and antimicrobial
Paradol	Phenolic Compound	Antioxidant, analgesic, and anti-inflammatory
Zingerone	Phenolic Compound	Antioxidant, anti-inflammatory, and antitumor
Globulin	Protein	Essential protein; impacts immune modulation and biological activity
Essential Oils	Oils	Antimicrobial, antiviral, antiparasitic, antiseptic, and antiallergic

A variety of clinical studies revealed an immunoregulatory pathology in ovarian cancer growth and invasion that are associated with suppressed cellular immunity and increased levels of blood Th2 cytokines and FoxP3+ T cells. Using ginger boosted the cell-mediated immune system, supported by the upregulation of the T helper 1 arm (from CD4 enhancement in the CD4/CD8 ratio), which facilitated the effectiveness of chemotherapy (via significant FoxP3 reduction and the decrease in the levels of its effector cytokine), thereby improving the outcome of the disease. All those findings agreed with those obtained in our previous related studies with the use of garlic. Complementary therapies remain a question for most oncologists. Increasing awareness of the effects of using naturally available herbals such as ginger will be of great importance and a note that must be emphasized in the practice of oncology [17-20]. Our aim in this work was to show that the use of ginger is complementary, and we investigated its effect on the immune cells in women with ovarian cancer and chemotherapy. Ginger was also seen to have a significant effect, and when patients used ginger during their chemotherapy sessions, there was an elevation in one type of T-helper cells, a significant increase in the ratio of one type of regulators of T lymphocytes (the other suppressor type is reduced in number), and a significant suppression of the suppressor cytokine and gene that promotes cancer growth (Figure 3). This decrease is seen as a result of the significant reduction in the number of reconstructed diseases and a significant decrease in the need for secondary surgery and additional chemotherapy. An example of highly significant changes in one of the patients is shown in tables. Tables illustrate data for a 41-year-old parous menopausal woman who was diagnosed with type ovarian cancer, stage In a follow-up of 6 months (Figure 1), it was noted that her recovery was progressing very well, with a significant increase in the level of HDL cholesterol and a decrease in the level of her triglycerides and chlorides. Her follow-up concentration of CA-125 also showed a significant decrease, indicating a good recovery. It was also noted that she did not need a second-look surgery at all. In addition, she was advised not to take any additional chemotherapy following the recommendation of the Gynecologic Oncologists committee in this hospital, as they found that her tissues were healing well and she was ready to stop therapy [12, 20-25].

Research is increasingly showing that ginger has the potential to induce a variety of health benefits, ranging from reducing nausea, vomiting, and inflammation to relieving pain, reducing fatigue, and enhancing cognitive function. Therefore, we sought to investigate

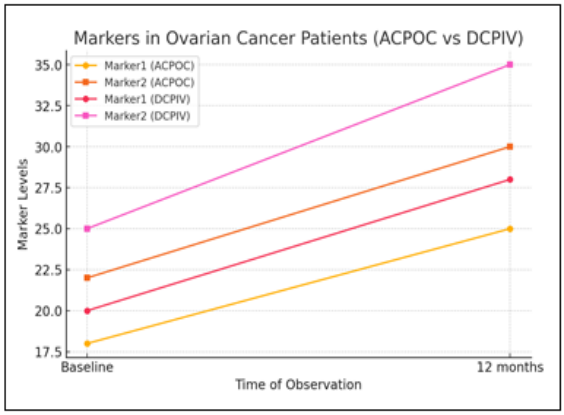

Figure 3. Show Outlining the Comparison of Immunological Markers among Patients with Ovarian Cancer in the Two Groups (ACPOC and DCPIV) and the Time of the Observation of the Follow-up, also in Different Colors

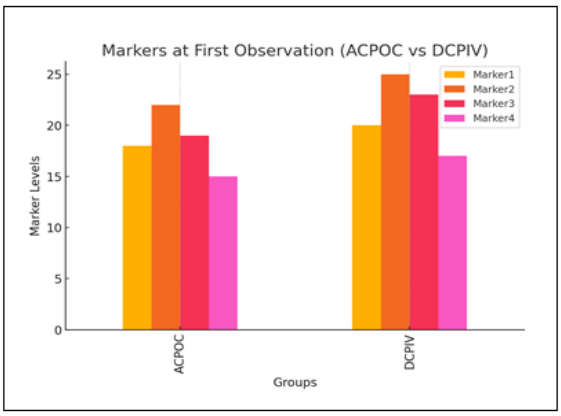

Figure 4. Showing the Comparison among all the Analyzed Immunological Markers for the First Time of Observation for ACPOC vs. DCPIV, which are also in different colors.

the physiological side of this multifaceted herb in order to understand to what extent we may anticipate ginger to influence a different, more general aspect of quality of life in this specific population. Ginger showed a unique role in elevating key metrics of physiological function in women with ovarian cancer. Averages were higher than the traditional therapeutic effects were anticipated. Physiological metrics were also clinically noticeably improved [26-31].

Our records coupled with the statements from the women in the present study suggested various unexpected behaviors, especially in relation to ginger's effect on improving energy and reducing pain. These findings are in accordance with the larger oncological subset of research, which found that these findings relate to clinical trials assessing ginger's antiemetic potential. This may be as a result of including individuals in that research whose NCP is a result of their cancer process, in contrast to the women in the present study who were suffering NCP from the possibly neurotoxic effects of chemotherapy. Our findings illustrate how ginger is capable of significantly enhancing a variety of important physiological parameters relative to standard care. The effect of ginger seemed to be both immediate and within thirty minutes it began to kick in to further lessen discomfort for the women in the present study. It is anticipated for ginger to diminish nausea and postoperative nausea specifically [31-39]

This is the first study conducted in Iraq to explore the potential physiological effect of Zingiber officinale as an adjuvant in ovarian cancer therapy in women. Approximately 20 studies were conducted to evaluate the features of Zingiber officinale in several malignancies. Ovarian cancer ranked sixth as the main aim in ginger therapy for ovarian, breast, gastric, prostate, B-cell leukemia, and colorectal cancer in cell culture and animal models. Of the conducted therapeutic cancer studies, 17 out of 20 used ginger in its natural form, and no intravenous trials were conducted [40-43].

In conclusion, this study details improvements in the immunological and physiological aspects of ovarian cancer in women objectively, which are reflected at the level of T cell activity and numbers. There is a reduction in LDH and serum inflammatory cytokines in the serum of ovarian cancer patients when treated with ginger clinically. Ginger can thus be considered a substance that could have a significant role in controlling ovarian cancer, in addition to playing a major role in enhancing automatic healing when undertaking courses of chemotherapy and radiotherapy, as well as reducing the side effects of chemotherapy and prolonging the lifetime of ovarian cancer patients (Figure 4).

Recommendation

This study supports the promising therapeutic application of ginger among cancer patients undergoing traditional cancer-related treatments. Larger multi-center randomized placebo-controlled trials may provide deeper insight into the variability of ginger administered with multiple treatment protocols and population demographics. Additionally, further research extends the continuation timeline to assess the long-term proliferative activity of various tumor gasoducts in the trained immunity state. We also encourage clinicians to consider collaborating in future nutritional, complementary, or natural timed nutrition studies to prevent contamination. The clinic team should remain blinded as much as possible to the project, while the dieticians are fully aware of the study's objectives. Hence, the variable time of treatment should be given to the clinicians, as the post-surgery pharmacotherapy is highly controlled in our oncology center.

Acknowledgments

The authors are thankful to Al-Ayen Iraqi University for the support provided to accomplish this study.

Funding

The authors of this manuscript did not receive any funding to perform the present research.

Conflict of interest

The authors of the study do not have any conflict of interest.

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