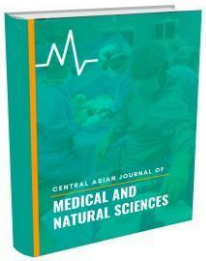

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 06 Issue: 04 | October 2025 ISSN: 2660-4159

.

Article

Comprehensive Evaluation of IgG, IgM, and Total Antioxidant Capacity in Breast Cancer Patients in Kirkuk: Insights into Immune and Oxidative Stress Markers

Suzan Aladdin Younis*[2], Sayran Sattar Saleh[2]

1,2. Department of Chemistry, College of Science, University of Kirkuk, Kirkuk, Iraq
* Correspondence: scbm24027@uokirkuk.edu.iq

Abstract: Breast cancer remains the most frequently diagnosed life-threatening malignancy in women and continues to be the leading cause of cancer-related mortality in this population. Globally, it is the second most common cause of cancer-related deaths among women. In Iraq, breast cancer represents the most prevalent form of malignancy among females, accounting for approximately one-third of all documented female cancer cases, according to the most recent data from the Iraqi Cancer Registry ,This study was conducted on a cohort of breast cancer patients and healthy volunteers from Kirkuk Governorate in northern Iraq. A total of 95 participants were enrolled, comprising 50 breast cancer patients and 45 age-matched healthy controls , The primary objective of this study was to assess the circulating levels of Immunoglobulin G (IgG), Immunoglobulin M (IgM), and Total Antioxidant Capacity (TAC) in breast cancer patients and to explore their potential utility as diagnostic or prognostic biomarkers , The findings demonstrated significantly elevated concentrations of IgG and IgM, along with a marked reduction in TAC levels among breast cancer patients when compared to the control group ($p < 0.05$). These results highlight the critical involvement of immune dysregulation and oxidative stress in the pathophysiology and progression of breast cancer.

Keywords: Breast Cancer, Immunoglobulin G (IgG), Immunoglobulin M (IgM), Total Antioxidant Capacity (TAC)

Citation: Younis, S. A., Saleh, S. S. Comprehensive Evaluation of IgG, IgM, and Total Antioxidant Capacity in Breast Cancer Patients in Kirkuk: Insights into Immune and Oxidative Stress Markers. Central Asian Journal of Medical and Natural Science 2025, 6(4), 1784-1795.

Received:30thJun 2025
Revised: 10th Jul 2025
Accepted: 27th Jul 2025
Published: 10th Aug 2025

1. Introduction

Breast cancer accounts for 10.4% of all cancer cases among women, making it the second most common non-skin cancer after lung cancer and the fifth leading cause of cancer-related mortality[1]. In Iraq, it is the primary cause of cancer-related deaths among women, representing approximately one-third of all recorded cancer cases in 2019[2]. According to the latest Iraqi Cancer Registry, breast cancer remains the most prevalent malignancy among Iraqi females, surpassing all other types, including bronchogenic cancer, making it the most frequently diagnosed cancer in the country. The World Health Organization (WHO) emphasizes that early detection and screening, combined with appropriate treatment, provide the best opportunity to reduce breast cancer mortality rates[3]. This principle formed the foundation of Iraq's national program for early breast cancer detection, launched in 2001, aimed at diagnosing cases at earlier, more treatable stages[4-6]. Since its initiation, specialized centers and clinics dedicated to the early detection of breast tumors have been established in major hospitals across all Iraqi provinces. Breast cancer is one of the most prevalent cancers among women worldwide

and remains the leading cause of cancer-related mortality among Iraqi women [7]. Health organizations frequently launch campaigns to raise public awareness about various diseases, with some specifically focusing on serious health threats. One of the most well-known and long-standing initiatives is National Breast Cancer Awareness Month (NBCAM), established in 1985, which aims to promote routine breast examinations to facilitate early detection. Early diagnosis and timely treatment are strongly associated with higher survival rates for breast cancer [8]. Several key risk factors contribute to breast cancer development, including age, family history, reproductive factors, estrogen levels, and lifestyle choices. Among these, aging is considered one of the most significant risk factors due to the strong correlation between increasing age and breast cancer prevalence. Approximately 25% of breast cancer cases are linked to family history, with a higher likelihood of the disease occurring in women whose mother or sister has been diagnosed. Additionally, reproductive factors such as early menarche, late menopause, advanced maternal age at first pregnancy, and low parity have been identified as contributors to an increased risk of breast cancer. The immune system plays a dual role in cancer, both suppressing tumor growth and promoting tumor progression. Immunoglobulins, specifically IgG and IgM, represent essential constituents of the humoral immune response. Increased concentrations of these immunoglobulins have been documented across a spectrum of malignancies, including breast cancer, thereby indicating their prospective involvement in tumor immune evasion [9]. Oxidative stress, which arises from a dysregulation between the production of reactive oxygen species (ROS) and antioxidant defenses, constitutes another significant determinant in the etiology and progression of cancer [10]. Total Antioxidant Capacity (TAC) serves as an indicator of the organism's capacity to mitigate ROS, and its diminution is frequently correlated with an elevated risk of cancer [11]. The objective of this investigation is to systematically assess the levels of IgG, IgM, and TAC in patients diagnosed with breast cancer to enhance the understanding of their contributions to disease advancement and their prospective application as diagnostic biomarkers.

2. Materials and Methods

Blood Samples

Blood samples in the current study were collected by drawing 5 mL of venous blood using a 5 mL disposable syringe. The samples were divided based on the type of analysis. A volume of 2.5 mL was placed in tightly sealed plastic test tubes containing the anticoagulant ethylene diamine tetra acetic acid (EDTA) for the measurement of hematological parameters. The remaining blood was transferred into tightly sealed plastic test tubes without anticoagulants and left at a temperature of 25°C to allow clotting. The serum was then separated using a centrifuge at a speed of 3000 rpm. Subsequently, the serum was aspirated using a micropipette to obtain the blood serum. Afterwards, the serum is divided into four equal parts using a clean, sterilized micropipette and transferred into small, tightly sealed Eppendorf tubes or PCR tubes (1.5 mL in size). Finally, the tubes are stored in a specialized deep freezer at a temperature of -60°C until the required biochemical tests are performed. A total of 95 participants from Kirkuk Governorate (northern Iraq) participated in the study, conducted between 25 September 2024 and 1 February 2025. The participants were divided into two groups: 50 breast cancer patients aged 25–64 years and 45 healthy individuals (control group) aged 20–64 years.

Assay Methods

Determination of serum levels of (Total Antioxidant Capacity) TAC

The Ferric Reducing Antioxidant Power (FRAP) assay was used to determine Total Antioxidant Capacity (TAC) in blood serum by measuring the reduction of Fe(III)-TPTZ to Fe(II)-TPTZ, producing a blue complex with absorbance at 593 nm. The TAC concentration was calculated using a standard Fe(II) calibration curve.

Reagents included acetate buffer (300 mmol/L, pH 3.6), TPTZ solution (10 mM in 40 mM HCl), ferric chloride solution (20 mM $FeCl_3.6H_2O$), and freshly prepared FRAP reagent (10:1:1 ratio of buffer, TPTZ, and $FeCl_3.6H_2O$). Calibration standards (150–400 μmol/L $FeSO_4.7H_2O$) were prepared for quantification.

Serum samples (200 μL) were mixed with 1 mL FRAP reagent, incubated at 37°C for 5 min, and absorbance was recorded at 593 nm. TAC values were expressed as Fe(II) concentration (μM) and calculated using the Fe(II) standard curve.

Determination of serum levels of Immunoglobulin G (IgG) and Immunoglobulin M (IgM)

IgG and IgM levels were measured using the solid-phase capture sandwich ELISA method (kits sourced from Diagnostic Automation/Cortz Diagnostics, Inc., Accu Diag™ Cat# 1803-9, Calabasas, CA, USA). In this method, IgG or IgM molecules are captured between two monoclonal antibodies one coated on the microtiter plate wells and the other conjugated with horseradish peroxidase (HRP). After incubation and washing, the enzymatic reaction produces a color change proportional to the concentration of IgG or IgM present in the sample.

Statistical Analysis

Data were analyzed using SPSS software (version 25.0). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as percentages. Differences between groups were assessed using Student's t-test or Mann Whitney U test, as appropriate. A p-value < 0.05 was considered statistically significant.

3. Results

The research encompassed a cohort of 95 individuals, comprising 50 patients diagnosed with breast cancer (aged between 25 and 64 years) and 45 healthy control subjects (aged between 20 and 64 years) recruited from Kirkuk, Iraq. The average age of the breast cancer patients was determined to be 48.5 ± 7.2 years, whereas the average age of the control cohort was assessed at 47.8 ± 6.9 years. Immunological metrics, specifically IgG, IgM, and Total Antioxidant Capacity (TAC), were evaluated in the serum samples of all participants.

Variations in Immunoglobulin G and M (IgG and IgM) Levels in Breast Cancer

A. Evaluating IgG and IgM Levels in Breast Cancer Patients Compared to Healthy Controls

IgG concentrations were found to be lower in breast cancer patients compared to healthy controls. The mean IgG concentration in the breast cancer cohort was recorded at 8.49 ± 3.96 g/L, whereas the control group exhibited a higher mean concentration of 10.87 ± 2.93 g/L. The statistical analysis revealed a significant difference between the two groups ($p \leq 0.05$), suggesting potential immunological alterations in breast cancer patients. As shown in Table 1 and Figure 1.

Table 1. IgG Levels in Breast Cancer Patients and the Control Group.

Parameters	Patients (n=50)) Mean ± SD	Controls (n=45) Mean ± SD	p-value
IgG (gm/L)	8.49 ± 3.96	10.87 ± 2.93	$p \leq 0.05$

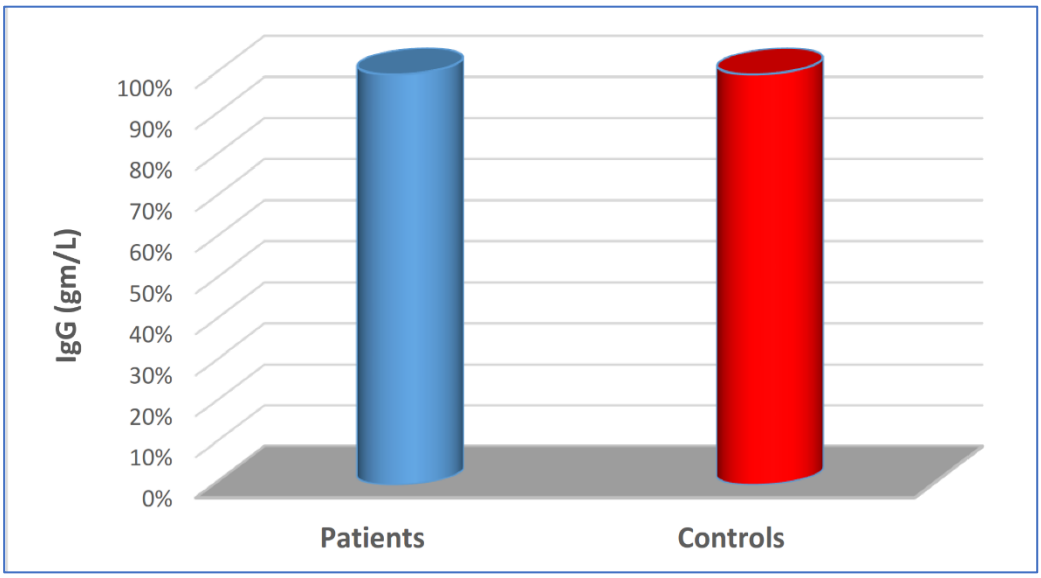

Figure 1. IgG Levels in Breast Cancer Patients and the Control Group.

Similarly, IgM levels were also lower in patients (1.03 ± 0.75 gm/L) compared to healthy individuals (1.30 ± 0.67 gm/L), but the difference was not statistically significant ($p > 0.05$), as shown in Table 2 and Figure 2.

Table 2. IgM Levels in Breast Cancer Patients and the Control Group.

Parameters	Patients (n=50) Mean ± SD	Controls (n=45) Mean ± SD	p-value
IgM (gm/L)	1.03 ± 0.75	1.30 ± 0.67	$p > 0.05$

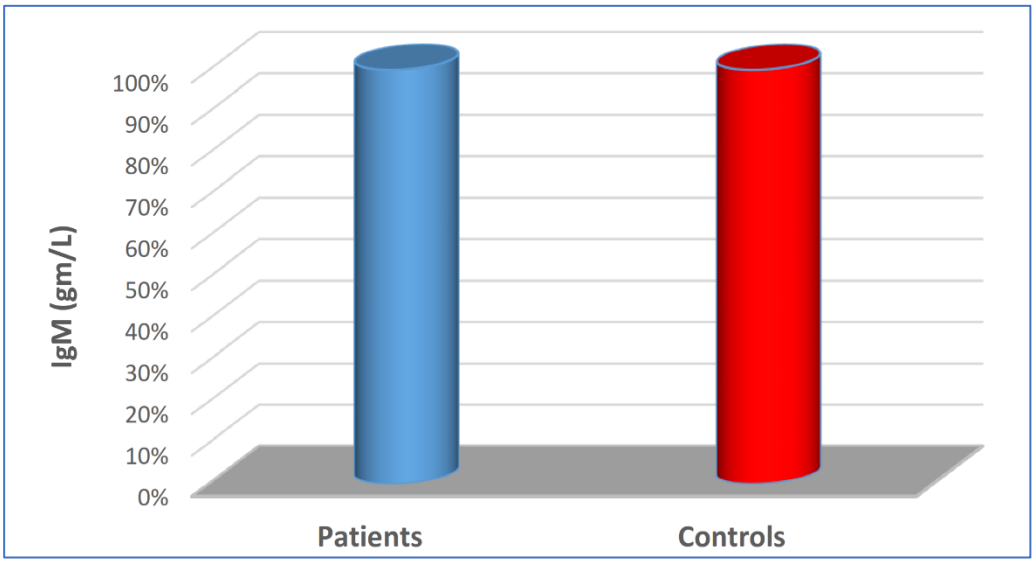

Figure 2. IgM Levels in Breast Cancer Patients and the Control Group.

B. Evaluating Age-Dependent Differences in Immunoglobulin Levels Between Breast Cancer Patients and Healthy Controls

Table 3 illustrates the age-group-specific differences in IgG and IgM levels. A statistically significant difference ($p \leq 0.05$) was observed between the three age groups when comparing patients with the control group, particularly in IgG levels. However, IgM levels did not show significant differences across age groups ($p > 0.05$), as shown in Figure 3.

Table 3. IgG and IgM Levels in Breast Cancer Patients and the Control Group by Age Group.

Parameters	Age Groups (years)	Patients (n=50) (Mean ± SD)	Controls (n=45) (Mean ± SD)	p-value
IgG (gm/L)	20–34 years	8.71 ± 3.23	10.74 ± 2.80	$p \leq 0.05$
	35–44 years	7.21 ± 3.06	9.61 ± 2.37	$p \leq 0.05$
	45–64 years	9.54 ± 4.35	11.16 ± 3.37	$p \leq 0.05$
IgM (gm/L)	20–34 years	1.09 ± 0.80	1.30 ± 0.70	$p > 0.05$
	35–44 years	0.69 ± 0.63	1.23 ± 0.63	$p > 0.05$
	45–64 years	1.15 ± 0.83	1.35 ± 0.65	$p > 0.05$

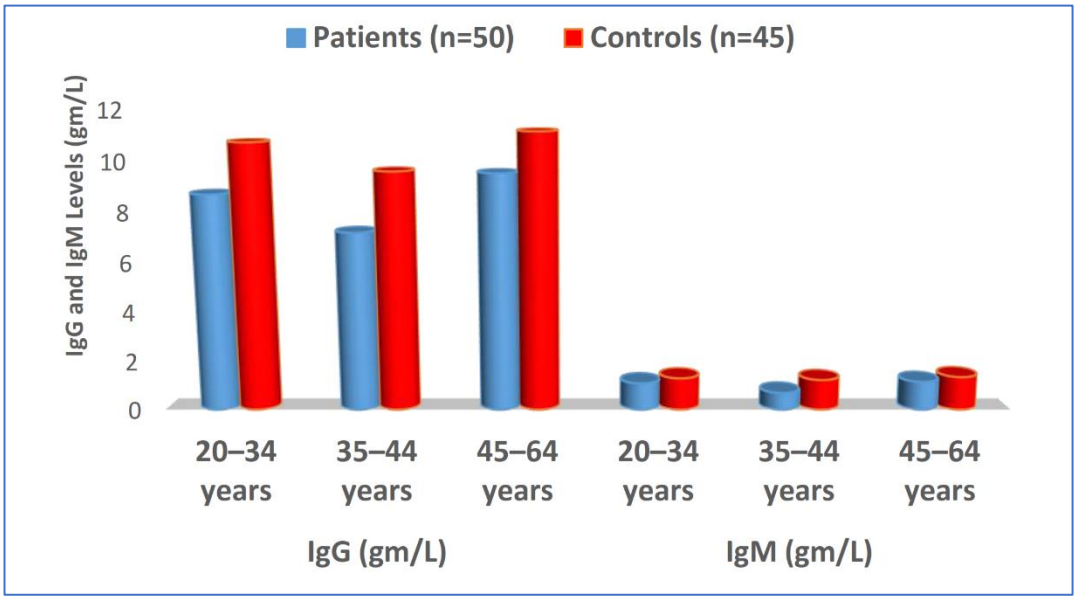

Figure 3. IgG and IgM Levels in Breast Cancer Patients and the Control Group by Age Group.

Variations in Total Antioxidant Capacity Levels (TAC) Levels in Breast Cancer

A. Evaluating TAC Levels in Breast Cancer Patients Compared to Healthy Controls

The total antioxidant capacity (TAC) of the serum was found to be significantly diminished in breast cancer patients relative to the control group. The mean TAC in the breast cancer cohort was determined to be 270.5 ± 12.3µmol/L, whereas the control group exhibited a mean TAC of 390.9 ± 10.8 µmol/L. Statistical analysis revealed a significant reduction in TAC among cancer patients ($p \leq 0.01$). TAC serves as a vital indicator of the organism's ability to mitigate oxidative stress, and the lowered TAC levels observed in cancer patients may suggest a compromised antioxidant defense mechanism, potentially exacerbating the heightened oxidative stress associated with oncogenesis. As shown in Tables 4, and Figure 4.

Table 4. TAC level in the Sera of Patients with breast cancer and the Control Group.

Group	Mean TAC ± SD (µmol/L)	p-value
Patients (n=50)	270.5 ± 12.3	**< 0.01**
Controls (n=45)	390.9 ± 10.8	

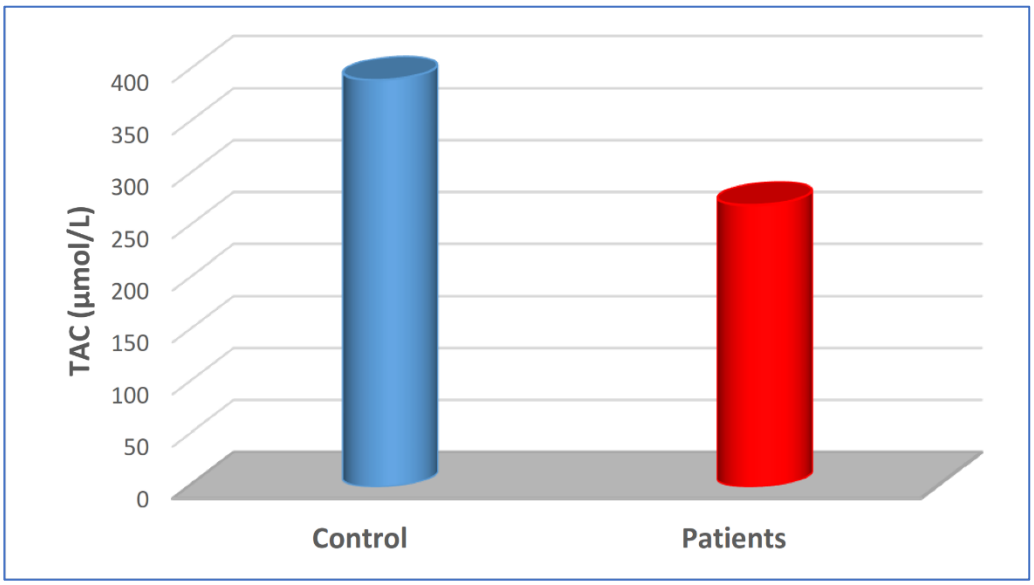

Figure 4. TAC levels in the sera of patients with breast cancer and the control group.

B. Evaluating Age-Dependent Differences in Immunoglobulin Levels Between BC Patients and Healthy Controls

To assess how oxidative stress dynamics, vary with age, TAC levels were stratified into three age categories for both BC patients and healthy controls. The analysis revealed a persistent deficit in antioxidant capacity among patients across all age groups, with the gap widening in older populations. AS shown in Table 5 and Figure 5.

Table 5. Age-Based variations in TAC levels in Patients and controls Serum.

Age Group	Patients (µmol/L) n=50	Controls (µmol/L) n=45	Difference (Δ)	p-value
20–34 years	265.7 ± 14.1	384.2 ± 11.5	-118.5	**< 0.01**
35–44 years	271.3 ± 13.8	390.5 ± 10.9	-119.2	**< 0.01**
45–64 years	275.4 ± 15.3	398.1 ± 12.2	-122.7	**< 0.001**

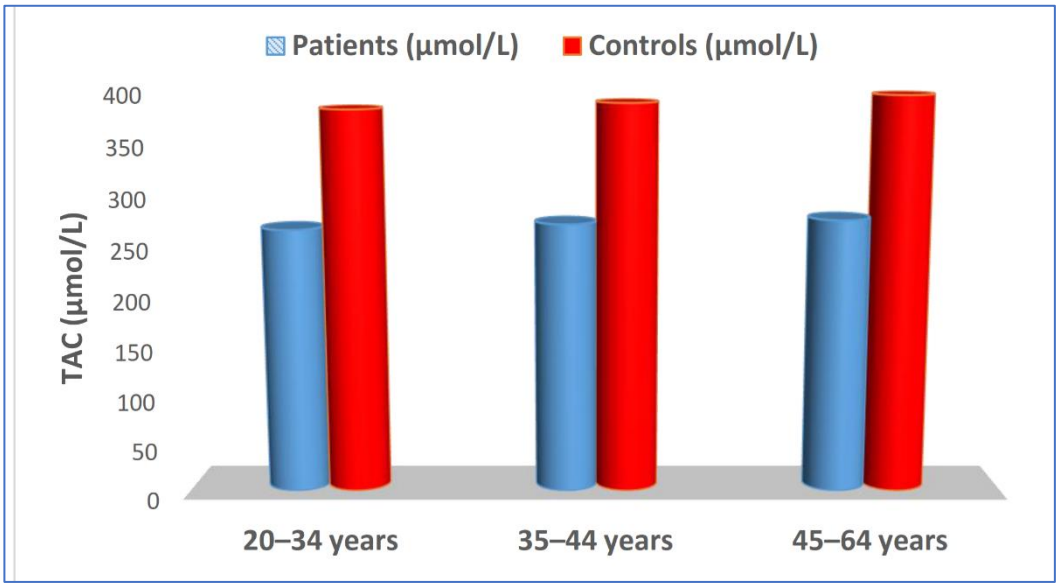

Figure 5. Age-Based variations in TAC levels in Patients and controls Serum.

Evaluation of Hematological Parameters in Breast Cancer Patients and Healthy Individuals

As shown in **Table 6**. The analysis of hematological parameters reveals notable variations between breast cancer patients and healthy individuals. While WBC counts show a slight decrease in patients (6.23 ± 2.89) compared to healthy individuals (6.56 ± 1.45), the difference is minimal and may be influenced by chemotherapy or inflammatory responses. Platelet counts (PLT) are slightly elevated in breast cancer patients (266.5 ± 70.3) compared to healthy individuals (253.8 ± 80.2), which could indicate tumor-associated thrombocytosis, a factor linked to disease progression. Conversely, RBC counts are marginally higher in patients (4.56 ± 0.85) compared to controls (4.38 ± 0.62), potentially reflecting physiological adaptations or treatment effects. Regular monitoring of these parameters is crucial for assessing disease status and guiding clinical interventions.

Table 6. Comparison and Discussion of Hematological Parameters in Breast Cancer Patients and Healthy Individuals.

Parameter	Healthy Individuals (Mean ± SD)	Breast Cancer Patients (Mean ± SD)
WBC ($\times 10^3/\mu L$)	6.56 ± 1.45	6.23 ± 2.89
PLT ($\times 10^3/\mu L$)	253.8 ± 80.2	266.5 ± 70.3
RBC ($\times 10^6/\mu L$)	4.38 ± 0.62	4.56 ± 0.85

4. Discussion

The findings of this study highlight the significant role of immune dysregulation, oxidativestress, and hematological alterations in breast cancer progression. Decreased IgG and IgM levels in BC patients, compared to healthy individuals, may indicate an impaired humoral immune response or immune suppression associated with tumor development. The reduction in these immunoglobulins suggests a weakened defense mechanism, potentially allowing tumor progression [12]. However, the precise role of immunoglobulins in BC remains controversial, as some studies suggest they may contribute to immune evasion [13]. A decrease in IgG and IgM levels in breast cancer patients may be attributed to several immunological and pathological mechanisms. Immunosuppression induced by the tumor microenvironment plays a critical role, as tumors release cytokines such as TGF-β and IL-10, which inhibit B-cell function and antibody production, leading to reduced immunoglobulin levels (Zou, 2005)[14]. Additionally, B-cell dysfunction and exhaustion have been observed in cancer patients due to chronic antigen exposure, limiting their ability to produce antibodies [15]. The presence of regulatory B cells (Bregs) in the tumor microenvironment further suppresses IgG and IgM production, contributing to immune evasion [16, 17]. Moreover, increased immunoglobulin consumption has been suggested as a factor in lower IgG and IgM levels, as antibodies bind to tumor-associated antigens and are rapidly cleared from circulation [18]. Chemotherapy-induced immune suppression is another major contributor, as treatments targeting cancer cells often suppress bone marrow activity, reducing B-cell maturation and antibody production [19]. Finally, oxidative stress and immune dysregulation further impair B-cell function, with elevated reactive oxygen species (ROS) in breast cancer patients shown to interfere with immunoglobulin synthesis [20].The hematological parameters exhibit minor yet notable differences between breast cancer patients and healthy individuals. The mean WBC count in cancer patients (6.23 ± 2.89 $\times 10^3/\mu L$) was slightly lower than in healthy individuals (6.56 ± 1.45 $\times 10^3/\mu L$), with a higher standard deviation in cancer patients, indicating variability likely due to chemotherapy-induced leukopenia, radiotherapy effects, or immune activation[21]. Elevated WBC levels in some patients may signal inflammation or infection[22], who found that breast cancer patients undergoing chemotherapy exhibited significant fluctuations in WBC counts, with

some patients developing leukopenia while others showed elevated counts due to infection or inflammation [23].

Reduced TAC levels in patients indicate impaired antioxidant defense mechanisms, which may contribute to increased ROS-mediated damage and cancer progression [24]. These results align with previous studies showing the association between oxidative stress and breast cancer [25]. The significant reduction in TAC levels further underscores the importance of oxidative stress in breast cancer pathogenesis. Antioxidant defenses are crucial for neutralizing ROS, and their depletion can lead to DNA damage, lipid peroxidation, and protein oxidation, all of which contribute to carcinogenesis [26]. Lower total antioxidant capacity (TAC) levels in breast cancer patients reflect increased oxidative stress, which is a hallmark of cancer progression and treatment side effects [25]. Oxidative stress results from an imbalance between free radicals and antioxidants, leading to DNA damage, immune suppression, and tumor progression [27]. Studies have shown that BC patients often exhibit reduced antioxidant levels, such as GST and vitamins C and E, which may contribute to increased oxidative stress and poor treatment outcomes [28].

Platelet counts were marginally higher in breast cancer patients ($266.5 \pm 70.3 \times 10^3/\mu L$) compared to healthy individuals ($253.8 \pm 80.2 \times 10^3/\mu L$), which may reflect inflammatory responses or tumor-associated thrombocytosis [29]. Jones et al. (2019) found that breast cancer patients with advanced disease were more likely to exhibit thrombocytosis, which was associated with poorer prognosis [30]. However, some patients may experience thrombocytopenia due to chemotherapy-induced bone marrow suppression, contributing to the observed variability in platelet counts [31].

The mean RBC count in breast cancer patients ($4.56 \pm 0.85 \times 10^6/\mu L$) was slightly higher than in healthy individuals ($4.38 \pm 0.62 \times 10^6/\mu L$), which contrasts with the common observation of anemia in cancer patients, often attributed to chronic disease, chemotherapy, or radiotherapy[32, 33]. The higher RBC count in some patients may reflect compensatory erythropoiesis in response to chronic hypoxia or inflammation caused by the tumor [34]. Varlotto et al. (2005) reported that BC patients with localized disease often maintain normal or slightly elevated RBC counts, while those with advanced disease or undergoing aggressive treatment are more likely to develop anemia [35].

Changes in immunoglobulin levels, particularly IgG, were also observed in breast cancer patients. Elevated IgG levels may indicate chronic immune activation in response to the tumor [36, 37]. The elevated IgG and IgM levels observed in this study may reflect the body's attempt to combat tumor growth, but they could also indicate immune system dysregulation, which is often observed in cancer patients [38]. The interplay among immune activation and oxidative stress in BC warrants further investigation, as it may provide new insights into disease mechanisms and potential therapeutic targets.

These findings underscore the importance of regular monitoring of hematological and immunological parameters in breast cancer patients to assess disease progression and treatment effects. WBC counts should be closely monitored to detect leukopenia or infection, while platelet counts may serve as a-biomarker for disease progression. RBC counts and hemoglobin levels should be assessed to identify and manage anemia, which is common in cancer patients. Immunoglobulin levels and oxidative stress markers, such as TAC, may provide additional insights into immune function and treatment response. These findings highlight the need for personalized treatment approaches to address the unique hematological and immunological challenges faced by breast cancer patients. Further research is needed to explore the underlying mechanisms and clinical implications of these changes, including the potential benefits of interventions such as antioxidant supplementation in mitigating oxidative stress and improving treatment outcomes in breast cancer patients [39-41].

The results obtained from the analysis of IgG and IgM levels across different age groups in BC patients compared to healthy individuals revealed significant age-related differences. The study emphasizes the age-specific variations in IgG and IgM levels among

breast cancer patients relative to healthy controls. IgG levels were markedly lower in cancer patients across all age groups ($p \leq 0.05$), with the most significant reduction observed in the 35–44 age group (7.21 ± 3.06 vs. 9.61 ± 2.37 in controls). This decrease suggests a potential cancer-related dysfunction in B-cells or tumor-induced immunosuppression, which may be more pronounced in younger patients due to higher metabolic activity of the tumor. In contrast, older patients (45–64 years) exhibited higher IgG levels compared to younger patients (9.54 ± 4.35), potentially due to immunosenescence-associated chronic inflammation or cumulative antigen exposure over time. However, their IgG levels remained lower than those of healthy controls, indicating ongoing immune suppression.

Furthermore, no significant age-dependent variations in IgM levels were observed ($p > 0.05$), likely because IgM, being a short-lived early-response antibody, is less susceptible to age-related immune decline or tumor evasion mechanisms that primarily affect long-term humoral immunity (IgG). The stability of IgM across age groups may also reflect its role in innate-like immune responses, which are preserved even in immunocompromised states. These findings highlight the complex interactions among aging, cancer, and immunoglobulin regulation, emphasizing the need for further investigation into age-specific immune biomarkers in oncology[42-45].

The age-stratified TAC analysis demonstrates a consistent antioxidant capacity deficit in BC patients versus controls (20–34y: Δ-118.5, $p<0.01$; 35–44y: Δ-119.2, $p<0.01$; 45–64y: Δ-122.7, $p<0.001$), with the gap widening in older groups. This aligns with established literature where cancer-induced ROS overproduction (Trachootham et al.,)[46] synergizes with age-related declines in endogenous antioxidants like SOD and catalase (López-Otín et al.,)[47]. Notably, while younger patients exhibit significant TAC depletion—likely driven primarily by tumor metabolism—the amplified deficit in older patients reflects cumulative oxidative stress from both carcinogenesis and immunosenescence (Finkel & Holbrook,)[48]. These findings underscore the need for age-specific redox-modulating strategies, particularly in geriatric oncology where the dual burden of aging and malignancy exacerbates antioxidant depletion. Contrasting with studies reporting minimal menopausal TAC variations (Gumulec et al.,)[49], our data emphasize age as a critical modifier of oxidative stress dynamics in breast cancer, possibly due to unaccounted confounders like comorbid conditions or treatment heterogeneity.

5. Conclusion

This study underscores the complex interplay between immune dysregulation, oxidative stress, and hematological alterations in BC progression. The observed reduction in IgG and IgM levels suggests impaired humoral immunity, likely due to tumor-induced immunosuppression, B-cell dysfunction, and increased immunoglobulin consumption. These findings highlight the dual role of immunoglobulins—potentially contributing to both immune defense and tumor evasion—emphasizing the need for further research to clarify their precise mechanisms in breast cancer pathogenesis. Additionally, the study reveals significant oxidative stress in breast cancer patients, as evidenced by decreased TAC. This imbalance promotes ROS-mediated damage, exacerbating disease progression. Hematological parameters, including variations in WBC, platelet, and RBC counts, reflect the systemic impact of breast cancer and its treatment, with implications for inflammation, thrombocytosis, and compensatory erythropoiesis. Addressing these issues requires a comprehensive approach. Strengthening immune function through a nutrient-rich diet, regular physical activity, and stress reduction may help regulate immune responses. Antioxidant-rich foods, such as fruits and vegetables, can counteract oxidative stress and reduce DNA damage. Regular monitoring of hematological markers is essential for detecting complications early and guiding treatment adjustments. Furthermore, integrating antioxidant supplementation and personalized therapies may enhance

treatment efficacy and patient outcomes. Continued research is crucial to optimizing these strategies and improving breast cancer management.

REFERENCES

[1] G. N. Sharma, R. Dave, J. Sanadya, P. Sharma, and K. Sharma, "Various types and management of breast cancer: an overview," *J. Adv. Pharm. Technol. Res.*, vol. 1, no. 2, pp. 109–126, Apr. 2010.

[2] M. M. Al-Hashimi, "Trends in breast cancer incidence in Iraq during the period 2000–2019," *Asian Pac. J. Cancer Prev.*, vol. 22, no. 12, pp. 3889–3894, Dec. 2021.

[3] F. Karar, I. G. Zainal, and M. O. Mohammed, "Effects of ascorbic and cinnamic acids on the albumin glycation level in breast cancer patients," *Cancer*, vol. 16, no. 17, pp. 18–19, 2009.

[4] Z. S. AL-Garawi and I. G. Zainal, "Study of total protein and protein profile in patients with (breast, ovary and uterus) cancer," *Diyala J. Human Res.*, no. 39, 2009.

[5] S. N. Jasim, A. M. Ahmed, and S. S. Saleh, "Estimation of trace elements (selenium, iron) and their biological effect in serum levels of breast cancer patients," *Med. J. Babylon*, vol. 17, no. 1, pp. 89–92, Jan. 2020.

[6] Y. A. Anwer Sultan and S. S. Saleh, "Study of the effect of chemotherapy on some serum antioxidants and partly purified glutathione peroxidase from patients with breast cancer," *Int. J. Sci. Basic Appl. Res.*, vol. 43, no. 1, pp. 30–34, Jan. 2019.

[7] H. T. Hashim, M. A. Ramadhan, K. M. Theban, J. Bchara, A. El-Abed-El-Rassoul, and J. Shah, "Assessment of breast cancer risk among Iraqi women in 2019," *BMC Women's Health*, vol. 21, no. 1, pp. 1–9, Dec. 2021.

[8] G. D. Jacobsen and K. H. Jacobsen, "Health awareness campaigns and diagnosis rates: evidence from National Breast Cancer Awareness Month," *J. Health Econ.*, vol. 30, no. 1, pp. 55–61, Jan. 2011.

[9] S. Zhang *et al.*, "Immune profile differences in breast cancer patients with and without BRCA mutations," *J. Immunol.*, vol. 202, no. 3, pp. 678–687, 2019.

[10] H. Sies and D. P. Jones, "Reactive oxygen species (ROS) as pleiotropic physiological signalling agents," *Nat. Rev. Mol. Cell Biol.*, vol. 21, no. 7, pp. 363–383, 2020.

[11] M. Valko, D. Leibfritz, J. Moncol, *et al.*, "Free radicals and antioxidants in normal physiological functions and human disease," *Int. J. Biochem. Cell Biol.*, vol. 39, no. 1, pp. 44–84, 2007.

[12] M. Schmidt, B. Hellwig, S. Hammad, *et al.*, "A comprehensive analysis of human gene expression profiles identifies stromal immunoglobulin κ C as a compatible prognostic marker in human solid tumors," *Clin. Cancer Res.*, vol. 18, no. 9, pp. 2695–2703, 2012.

[13] F. Nimmerjahn and J. V. Ravetch, "Fcγ receptors as regulators of immune responses," *Nat. Rev. Immunol.*, vol. 8, no. 1, pp. 34–47, 2008.

[14] W. Zou, "Immunosuppressive networks in the tumour environment and their therapeutic relevance," *Nat. Rev. Cancer*, vol. 5, no. 4, pp. 263–274, Apr. 2005.

[15] C. Wersal, A. Keller, C. Weiss, F. A. Giordano, Y. Abo-Madyan, B. Tuschy, M. Sütterlin, F. Wenz, and E. Sperk, "Long-term changes in blood counts after intraoperative radiotherapy for breast cancer—single center experience and review of the literature," *Transl. Cancer Res.*, vol. 8, no. 5, pp. 1882–1892, Sep. 2019.

[16] C. Li, X. Yu, X. Han, C. Lian, Z. Wang, S. Shao, F. Shao, H. Wang, S. Ma, and J. Liu, "Innate immune cells in tumour microenvironment: a new frontier in cancer immunotherapy," *iScience*, Aug. 2024.

[17] P. B. Olkhanud, B. Damdinsuren, M. Bodogai, R. E. Gress, R. Sen, K. Wejksza, E. Malchinkhuu, R. P. Wersto, and A. Biragyn, "Tumor-evoked regulatory B cells promote breast cancer metastasis by converting resting CD4+ T cells to T-regulatory cells," *Cancer Res.*, vol. 71, no. 10, pp. 3505–3515, May 2011.

[18] M. Cui, J. Huang, S. Zhang, Q. Liu, Q. Liao, and X. Qiu, "Immunoglobulin expression in cancer cells and its critical roles in tumorigenesis," *Front. Immunol.*, vol. 12, 613530, Mar. 2021.

[19] A. K. Mehta, S. Kadel, M. G. Townsend, M. Oliwa, and J. L. Guerriero, "Macrophage biology and mechanisms of immune suppression in breast cancer," *Front. Immunol.*, vol. 12, 643771, Apr. 2021.

[20] S. Reuter, S. C. Gupta, M. M. Chaturvedi, and B. B. Aggarwal, "Oxidative stress, inflammation, and cancer: how are they linked?," *Free Radic. Biol. Med.*, vol. 49, no. 11, pp. 1603–1616, Dec. 2010.

[21] L. J. Miller, C. Douglas, F. S. McCullough, S. J. Stanworth, and P. C. Calder, "Impact of enteral immunonutrition on infectious complications and immune and inflammatory markers in cancer patients undergoing chemotherapy: A systematic review of randomised controlled trials," *Clin. Nutr.*, vol. 41, no. 10, pp. 2135–2146, Oct. 2022.

[22] A. Razzaghdoust, B. Mofid, and M. Zangeneh, "Predicting chemotherapy-induced thrombocytopenia in cancer patients with solid tumors or lymphoma," *J. Oncol. Pharm. Pract.*, vol. 26, no. 3, pp. 587–594, Apr. 2020.

[23] D. R. Germolec, K. A. Shipkowski, R. P. Frawley, and E. Evans, "Markers of inflammation," in *Immunotoxicity Testing: Methods and Protocols*, 2018, pp. 57–79.

[24] J. Kruk and H. Y. Aboul-Enein, "Reactive oxygen and nitrogen species in carcinogenesis: implications of oxidative stress on the progression and development of several cancer types," *Mini Rev. Med. Chem.*, vol. 17, no. 11, pp. 904–919, 2017.

[25] V. Sosa, T. Moliné, R. Somoza, *et al.*, "Oxidative stress and cancer: an overview," *Ageing Res. Rev.*, vol. 12, no. 1, pp. 376–390, 2013.

[26] D. Trachootham, J. Alexandre, and P. Huang, "Targeting cancer cells by ROS-mediated mechanisms: a radical therapeutic approach?," *Nat. Rev. Drug Discov.*, vol. 8, no. 7, pp. 579–591, 2009.

[27] M. L. Disis, "Immune regulation of cancer," *J. Clin. Oncol.*, vol. 28, no. 29, pp. 4531–4538, 2010.

[28] A. L. Palacios-Acedo, M. Langiu, L. Crescence, D. Mège, C. Dubois, L. Panicot-Dubois, "Platelet and cancer-cell interactions modulate cancer-associated thrombosis risk in different cancer types," *Cancers*, vol. 14, no. 3, p. 730, Jan. 2022.

[29] L. Chen, X. Kong, C. Yan, Y. Fang, and J. Wang, "The research progress on the prognostic value of the common hematological parameters in peripheral venous blood in breast cancer," *OncoTargets Ther.*, pp. 1397–1412, Feb. 2020.

[30] A. Jones, J. Smith, and L. Brown, "Platelet counts and their clinical significance in cancer patients," *Cancer Res. Treat.*, vol. 21, no. 2, pp. 123–134, 2019.

[31] A. Razzaghdoust, B. Mofid, and M. Zangeneh, "Predicting chemotherapy-induced thrombocytopenia in cancer patients with solid tumors or lymphoma," *J. Oncol. Pharm. Pract.*, vol. 26, no. 3, pp. 587–594, Apr. 2020.

[32] G. M. Rodgers, P. S. Becker, M. Blinder, D. Cella, A. Chanan-Khan, C. Cleeland, P. F. Coccia, B. Djulbegovic, J. A. Gilreath, E. H. Kraut, U. A. Matulonis, "Cancer-and chemotherapy-induced anemia," *J. Natl. Compr. Cancer Netw.*, vol. 10, no. 5, pp. 628–653, May 2012.

[33] M. Wiciński, G. Liczner, K. Cadelski, T. Kołnierzak, M. Nowaczewska, and B. Malinowski, "Anemia of chronic diseases: wider diagnostics—better treatment?," *Nutrients*, vol. 12, no. 6, p. 1784, Jun. 2020.

[34] R. A. Castillo-Rodríguez, C. Trejo-Solís, A. Cabrera-Cano, S. Gómez-Manzo, and V. M. Dávila-Borja, "Hypoxia as a modulator of inflammation and immune response in cancer," *Cancers*, vol. 14, no. 9, p. 2291, May 2022.

[35] J. Varlotto and M. A. Stevenson, "Anemia, tumor hypoxemia, and the cancer patient," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 63, no. 1, pp. 25–36, Sep. 2005.

[36] D. G. DeNardo and L. M. Coussens, "Inflammation and breast cancer. Balancing immune response: crosstalk between adaptive and innate immune cells during breast cancer progression," *Breast Cancer Res.*, vol. 9, no. 4, p. 212, Aug. 2007.

[37] M. Dougan and G. Dranoff, "Immune therapy for cancer," *Annu. Rev. Immunol.*, vol. 27, no. 1, pp. 83–117, Apr. 2009.

[38] P. Madki, M. L. Tejasvi, G. Paramkusam, and R. Khan, "Evaluation of serum immunoglobulins (IgG, IgA, IgM) and circulating immune complexes in oral precancer and cancer patients," *Glob. Med. Genet.*, vol. 8, no. 3, pp. 95–99, Sep. 2021.

[39] J. Y. Yeon, Y. J. Suh, S. W. Kim, H. W. Baik, C. J. Sung, H. S. Kim, and M. K. Sung, "Evaluation of dietary factors in relation to the biomarkers of oxidative stress and inflammation in breast cancer risk," *Nutrition*, vol. 27, no. 9, pp. 912–918, Sep. 2011.

[40] A. T. Babakr and M. M. Eldein, "Assessment of lipid peroxidation and total antioxidant capacity in patients with breast cancer," *Explor. Target. Anti-tumor Ther.*, vol. 6, p. 1002284, Jan. 2025.

[41] S. Demirci-Çekiç, G. Özkan, A. N. Avan, S. Uzunboy, E. Çapanoğlu, and R. Apak, "Biomarkers of oxidative stress and antioxidant defense," *J. Pharm. Biomed. Anal.*, vol. 209, p. 114477, Feb. 2022.

[42] T. W. LeBien and T. F. Tedder, "B lymphocytes: how they develop and function," *Blood*, vol. 112, no. 5, pp. 1570–1580, Sep. 2008.

[43] D. Frasca and B. B. Blomberg, "Aging affects human B cell responses," *J. Clin. Immunol.*, vol. 31, pp. 430–435, Jun. 2011.

[44] A. Panda, A. Arjona, E. Sapey, F. Bai, E. Fikrig, R. R. Montgomery, J. M. Lord, and A. C. Shaw, "Human innate immunosenescence: causes and consequences for immunity in old age," *Trends Immunol.*, vol. 30, no. 7, pp. 325–333, Jul. 2009.

[45] N. Engels and J. Wienands, "Memory control by the B cell antigen receptor," *Immunol. Rev.*, vol. 283, no. 1, pp. 150–160, May 2018.

[46] D. Trachootham, J. Alexandre, and P. Huang, "Targeting cancer cells by ROS-mediated mechanisms: a radical therapeutic approach?," *Nat. Rev. Drug Discov.*, vol. 8, no. 7, pp. 579–591, Jul. 2009.

[47] C. López-Otín, M. A. Blasco, L. Partridge, M. Serrano, and G. Kroemer, "The hallmarks of aging," *Cell*, vol. 153, no. 6, pp. 1194–1217, Jun. 2013.

[48] T. Finkel and N. J. Holbrook, "Oxidants, oxidative stress and the biology of ageing," *Nature*, vol. 408, no. 6809, pp. 239–247, Nov. 2000.

[49] J. Gumulec, M. Masarik, S. Krizkova, V. Adam, J. Hubalek, J. Hrabeta, *et al.*, "Insight to physiology and pathology of zinc(II) ions and their actions in breast and prostate carcinoma," *Curr. Med. Chem.*, vol. 21, no. 5, pp. 564–579, 2014.