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ORIGINAL STUDY

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Assessment of Serum Levels of Na, K, Mg, Fe^{+2}, and Se as Potential Risk Markers in Women with Breast Cancer

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Abstract

Background: Breast cancer is a malignant neoplasm characterized by uncontrolled proliferation of breast epithelial cells, with potential for metastasis.
Objectives: To follow the change in the level of trace elements (TEs) and the extent to which these changes are related to the risk of breast cancer before taking chemotherapy or removing the tumor.
Materials and Methods: The case-control group had 90 Iraqi women with newly diagnosed breast cancer, alongside 90 healthy women who were matched for age and body mass index. Elements and electrolytes in the serum, such as iron, sodium, potassium, magnesium, and selenium, were measured using a spectrophotometer. The statistical significance of the differences was determined using SPSS.
Results: The evaluation of electrolytes showed a significant increase in the concentrations of Na, K, in contrast to a significant decrease in the concentrations of Se and Mg in the breast cancer patients compared to the healthy control group. In the current study, among breast cancer patients, the concentration of Iron in the serum was significantly greater in patients with stage IV breast cancer. The Se level had a significant association with the degree of effectiveness in diagnosing breast cancer.
Conclusion: Trace elements and electrolytes can be used as biomarkers for the diagnosis of breast cancer, and further studies are needed to confirm the relationship between trace elements and breast cancer.Our study provides insights into the potential risk markers for breast cancer patients, especially in stage III and IV breast cancer, and the roles and effects of trace elements in breast cancer.

Keywords: Breast cancer, Metastasis, Trace elements

1. Introduction

Breast cancer is one of the most prevalent malignancies and the major cause of cancer-related death in women worldwide [1, 2]. Cancer cells can directly activate the blood-clotting cascade and cause thrombosis [3]. The incidence of breast cancer has steadily increased in the past years. With the improvements in early detection and treatment achieved, most women are diagnosed in the early stages of breast cancer [4]. The incidence of breast cancer is generally considered to be the interaction of environmental factors and genetic factors, and approximately 5–10% of breast cancers are inheritable [5].

The occurrence and development of breast cancer are related to a variety of physiological factors, including but not limited to age, menstrual status, fertility, breastfeeding, and obesity [6]. The early detection of breast cancer is helpful for early diagnosis. There are many trace elements that are part of

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metalloenzyme and play a vital role in biological functions, such as structure, the composition of macromolecules, oxygen transport, hormonal activities, and free radical scavenging [7]. potassium ion plays an important role in normal nerve transmission; it is necessary to have K+ transfer via the nerve cell membrane. The increased concentration of potassium ions or deficiencies can cause adverse effects in biological functions, such as heart function and electrocardiographic change, etc. [8] Iron is an essential trace element in the body due to it is very important for biological essential component of every living organism. Many metabolic processes such as oxygen transport, deoxyribonucleic acid (DNA) synthesis, the synthesis of neurotransmitters and electron transport, require iron. However, the concentration of iron in the tissues of the body must be tightly regulated to avoid the formation of reactive oxygen species (ROS), a natural reactions, because excessive amounts of iron can cause tissue damage [9], As such, both high dietary iron intake and elevated body iron status have been hypothesized to increase the risks of several cancers, including breast cancer [10].

Cellular oxidative damage is a general mechanism for cell and tissue injury. Oxidative stress in the target tissue has been suggested to play an important role in the carcinogenic process. Thus, Se may act as an antitumor agent, although more studies are needed to investigate the actual role of antioxidants and their possible relationships with trace element alterations in the pathogenesis of breast cancer [11, 12].

Moreover, a strong relationship between low-serum Se concentration and increased risk of breast cancer has been documented, Therefore, in this study, we simultaneously measured serum levels of trace elements in Najaf female breast cancer patients and compared these values with female controls without breast cancer using spectrophotometer. Furthermore, we investigated clinical and laboratory variables related to trace element levels in breast cancer patients. which were essential for predicting the progression and incidence of the disease [13, 14].

2. Materials and methods

The study was a case-control design with 180 volunteers aged 40 to 60 years, conducted between December 2024 and April 2025. All participants were divided into two groups: 90 individuals newly diagnosed with breast cancer at the following stages: Stage II (n = 43), Stage III (n = 31), and Stage IV (n = 16). The diagnosis was made by specialists at the Oncology Hospital in Najaf, Iraq, through mammography and histopathological examination. In addition, 90 healthy participants matched for age and BMI served as controls. Those with chronic diseases, autoimmune diseases, microbial infections, smokers, those taking oral contraceptives or hormonal medications, those undergoing surgery, and women who were pregnant or undergoing any medical treatment were excluded from the study.

Five mL of fasting blood (8–12 hours) was drawn from each patient's vein after breast cancer diagnosis but before initiating any treatment. The blood was centrifuged at 3,000 rpm for 10 minutes, with serum separated into four test tubes. It was then stored at -20° C until analysis. Serum sodium, potassium, magnesium, iron, and selenium concentrations were measured by the colorimetric methods using a spectrophotometer at different wavelengths. using kits from BIOLABO and HUMAN.Measurements included age, weight, height, waist circumference, and hip circumference. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of the individual's height in meters: BMI = (weight in kilograms) / (height in meters squared) [15].

3. Statistical analysis

Data were collected and analyzed using the IBM Statistical Package for Social Sciences version 27 (SPSS, Chicago, IL, USA). Results are expressed as (mean ± SD) of normally distributed values. The distribution type of the outcome groups was analyzed using the Kolmogorov-Smirnov test. Differences in scale variables between diagnostic categories were assessed using the Student's t-test. Differences in scale variables between diagnostic groups were assessed using the one-way analysis of variance (ANOVA) test. The Pearson correlation coefficient (r) assessed the relationship between a scale variable and a parameter to determine its association with another variable. Statistical significance for all hypothesis tests was determined with a p value ≤ 0.05. The diagnostic efficacy of the investigated biomarkers in diagnosing the disease was assessed using receiver operating characteristic (ROC) curves. The threshold concentration yielded the best sensitivity and specificity based on the area under the curve. (AUC).

3.1. Ethical approval

Prior to collecting study samples, the ethical guidelines for the procedures strictly adhered to the principles of the Declaration of Helsinki, with patients providing verbal and written informed consent before donating samples. The Institutional Review Board of the College of Science, University of Kufa, Iraq, approved the study methods, participant information, and permission form (approval number 4716

Table 1. Demographic and clinical data of breast cancer patients and healthy control groups.

Parameters	Patients group (mean ± SD)	Controls group (mean ± SD)	P- value
Number	90	90	——-
Age (years)	47.84 ± 9.271	47.67 ± 9.142	0.482
Height(cm^2)	158.82 ± 6.970	159.17 ± 4.579	0.665
Weight (kg/m^2)	70.09 ± 13.05	73.67 ± 11.684	0.290
BMI (kg/m^2)	26.82 ± 3.183	26.95 ± 3.938	0.509
Na (mmol/L)	142.77 ± 2.724	138.13 ± 4.133	0.0001
K (mmol/L)	5.391 ± 1.610	5.430 ± 2.199	0.947
Mg (mmol/ L)	2.027 ± 0.203	2.113 ± 0.355	0.169
Fe^{+2} ($\mu g/dL$)	281.29 ± 133.985	86 ± 36.789	0.0001
Se (mmol/ L)	2.275 ± 0.657	4.743 ± 0.676	0.0001

Data displayed as mean ± SD, where SD Standard Deviation, BMI: Body Mass Index, Na: Sodium, K: potassium, Mg: Magnesium, Fe^{+2}:Iron,Se: Selenium.

dated December 14, 2024), as well as the local ethics committee. Additional data approved by the hospital administration included demographics, medical history, exposure details, signs/symptoms, and laboratory results.

4. Results

The investigation contrasted 90 patients with newly diagnosed breast cancer with 90 healthy women in order to assess the various clinical characteristics listed in (Table 1) (mean ± standard deviation). Patients were between the ages of 40 and 60. Other trace elements exhibited a significant difference, with increased levels in breast cancer patients. All stages exhibited an increase in sodium, potassium, and iron, while a nonsignificant decrease in selenium and magnesium, was observed in breast cancer patients compared to healthy individuals, as documented in (Table 2).

The receiver operating characteristic of the analysis evaluated the reliability of Trace elements in diagnosing disease. Fig. 1 depicts the graphs constructed using the coordinate data, and the optimal sensitivity/specificity threshold values are listed in (Table 3). The levels of selenium demonstrated a significant capacity to diagnose efficacy in breast cancer patients, the cut-off value of 3,450 mmol/L achieved 100.0% sensitivity and 100.0% specificity (AUC 1.000, 95% CI: 1.000–1.000; P < 0.0001). The outcomes demonstrate the capacity of Trace elements to differentiate between breast cancer and other diseases.

Table 2. Comparison of variables between the stages of breast cancer patients.

	Patients Stages (No. = 90)		
variables	Stage II	Stage III	Stage IV
Number	43	31	16
Na (mmol/L)	140.586 ± 4.558	141.379 ± 5.175	144.757 ± 1.912
	p-value: a) 0.0001 b) 0.0001 c) 0.0001		
K (mmol/L)	5.077 ± 2.923	5.937 ± 3.682	5.328 ± 3.552
	p-value: a) 0.079 b) 0.082 c) 0.076		
Mg (mmol/L)	2.778 ± 0.168	2.714 ± 0.573	2.458 ± 0.601
	p-value: a) 0.051 b) 0.049 c) 0.326		
Fe^{+2} ($\mu g/dL$)	280.132 ± 130.06	280.31 ± 135.176	283.48 ± 110.601
	p-value: a) 0.05 b) 0.047 c) 0.472		
Se (mmol/L)	2.11 ± 0.651	2.03 ± 0.509	1.58 ± 0.536
	p-value: a) 0.05 b) 0.06 c) 0.481		

Data displayed as mean ± SD, where SD Standard Deviation, BMI: Body Mass Index, Na: Sodium, K: potassium, Mg: Magnesium, Fe^{+2}: Iron,Se: Selenium, Significant differences among stages: a) Stage II compared to Stage III, b) Stage II compared to Stage IV, c) Stage III compared to Stage IV.

5. Discussion

Trace elements have a significant impact on the conservation of body functions via their participation in numerous significant chemical reactions that occur in the body [16]. The levels of trace elements in biological fluids should be within appropriate limits because they are also known as causative agents which may contribute to growth and endocrine disorders. There are numerous studies in the literature that reveal the association between trace element status and certain diseases [17]. Sodium is one of the most important ions in the body and is involved in essential physiological processes, such as maintaining a balanced fluid composition and contracting muscles. Irregularities in sodium balance are the most common electrolyte disorders encountered in clinical practice [18].

On the other hand, the present results clearly show, as seen from previous studies that the concentration of sodium elements increases in cases of breast cancer blood in the human body [19].The role of sodium (compound form) in cancerous blood is also a significant concern. Magnesium is the second most prevalent intracellular cation and the fourth most abundant cation in the body. It is considered crucial to the body's molecular, biochemical, and physiological processes as well as to the cellular and enzymatic functioning of several organ systems [20]. In instances

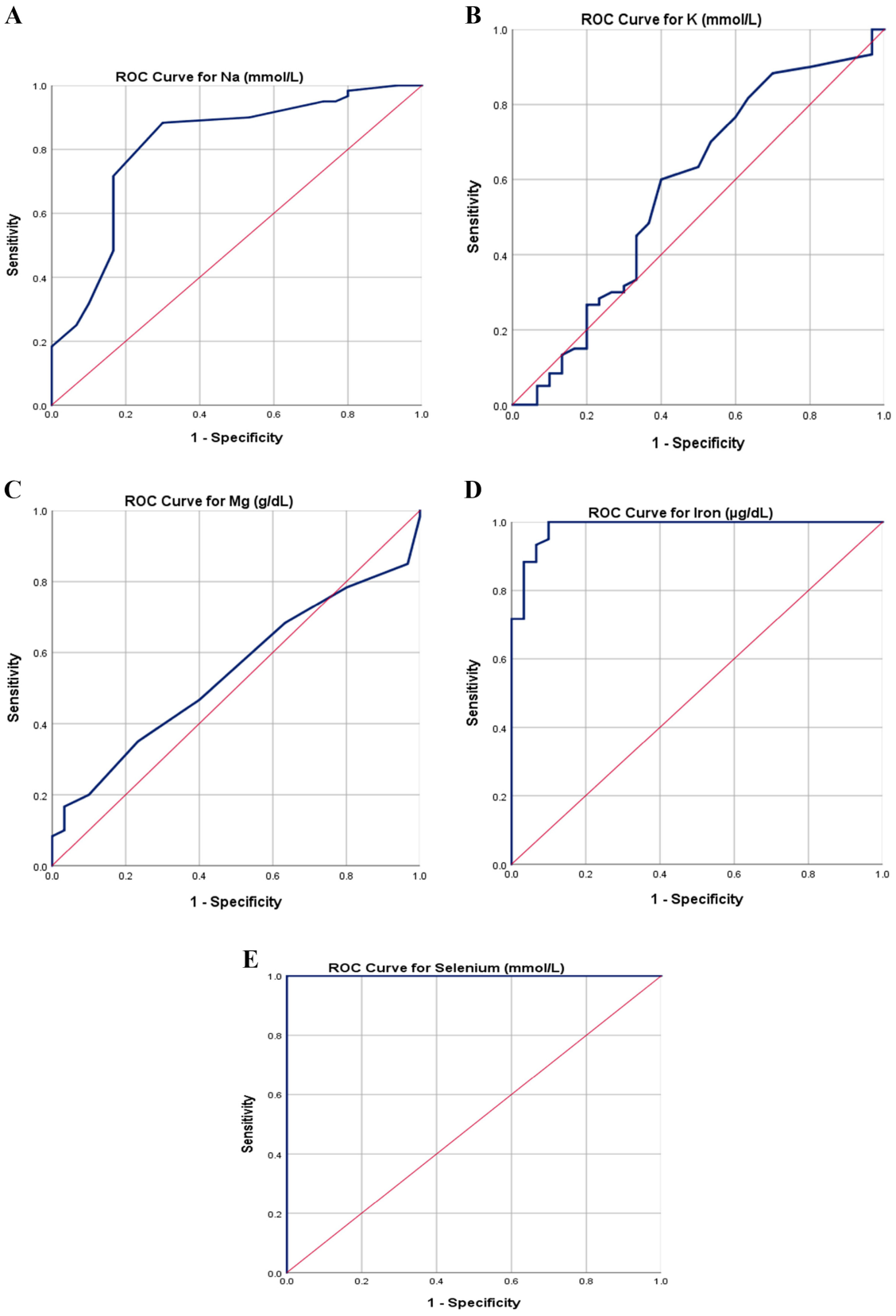

Fig. 1. Receiver operating characteristic curve for breast cancer patients A: Na, B: K, C: Mg, D: Iron, E: Selenium.

Table 3. Receiver operating characteristic-area under the curve analysis of the diagnosis for breast cancer patients vs. healthy control.

Variables	Cut-off concentration	Sensitivity %	Specificity %	AUC	95% CI of AUC	p-value
Na (mmol/L)	140.50	80.0	76.0	0.813	0.713–0.913	<0.0001
K (mmol/L)	4.75	60.0	60.0	0.578	0.445–0.711	<0.227
Mg (mmol/L)	2.05	52.3	51.8	0.543	0.423–0.663	<0.507
Iron (μg/dL)	127.000	98.3	99.0	0.985	0.963–1.000	<0.0001
Selenium (mmol/L)	3.450	100.0	100.0	1.000	1.000–1.000	<0.0001

of hypomagnesemia, increased levels of free radicals and inflammation may lead to DNA damage and mutations that cause cancer [21]. which highlights the significance of optimal concentrations of magnesium in intracellular and extracellular compartments. Previous studies have hypothesized an association between magnesium and breast cancer [22], Potassium is a major determinant of intracellular osmolality. The ratio between potassium concentration in the intracellular fluid (ICF) and concentration in the extracellular fluid (ECF) strongly influences cell membrane polarization, which in turn influences important cell processes, such as the conduction of nerve impulses and muscle (including myocardial) cell contraction. Thus, relatively small alterations in serum potassium concentration can have significant clinical manifestations [23]. The role of K+ in regulating the proliferation of tumor cells and as an anti-apoptotic and pro-apoptotic agent is well documented [24] .Iron is crucial to the activity of various proteins and enzymes involved in multiple biological processes [25]. However, iron also promotes oxidative stress; this can lead to DNA damage. Increasing numbers of studies have demonstrated that homeostatic alterations to iron metabolism and a shift in the distribution of iron in the serum are present in different types of cancer, these changes are associated with breast cancer [25, 26]. An overabundance of iron or iron deficiency due to a lack of regulation in iron homeostasis can facilitate the development, progression, and metastasis of cancer cells [27].

The current study, through a meta-analysis of the serum of women with breast cancer from Najaf, demonstrated a direct association between high iron levels and an increased risk of breast cancer. Similarly, a systematic review of the evidence concerning the association between Fe and breast cancer risk concluded that this element possesses a promotional role in breast cancer [28]. As a result, it was discovered that higher iron concentrations can increase the risk of breast cancer in women [29].

Selenium is an integral part of the antioxidant enzyme glutathione peroxidase; this enzyme can inhibit the production of cancerous cells and DNA. Se-containing molecules have the ability to antioxidants and participate in maintaining the equilibrium of a healthy body [30]. Epidemiological and preclinical evidence illustrate that Se is a trace element with anti-cancer activity and is associated with tumor growth, metastasis, angiogenesis, and drug resistance [31, 32]. Accumulated evidence demonstrates that Se possesses anti-cancer properties in the breast and that increased serum levels of Se can predict the survival of patients after breast cancer [33, 34]. indicating its potential as a natural anti-cancer therapeutic agent [35].

6. Conclusion

We first examined the levels of several trace elements and electrolytes in the serum of breast cancer patients in Najaf in a control group. Serum Na, K, and Fe^{2+} concentrations were significantly higher in breast cancer patients than in the control group ($p < 0.05$), while serum Se and Mg concentrations were significantly lower ($p < 0.05$). Se levels demonstrated significant diagnostic value in breast cancer patients, with the cut-off value 3.450 mmol/L.Our study provides insights into the potential risk markers for breast cancer patients, especially in stages III and IV, and the roles and effects of trace elements in breast cancer. Trace elements and electrolytes (Fe, Na, K, Mg, and Se) can be used as biomarkers for breast cancer diagnosis using ROC curves. Further studies are needed to confirm the relationship between trace elements and breast cancer.

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Declaration of interest

The authors declare no conflict of interest

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Ethical Approval

References

1. Tan L, *et al.* PIWI-interacting RNA-36712 restrains breast cancer progression and chemoresistance by interaction with SEPW1 pseudogene SEPW1P RNA. Molecular cancer. 2019;18(1):9.
2. Duijf, Pascal HG, *et al.* Mechanisms of genomic instability in breast cancer. Trends in molecular medicine. 2019;25(7):595–611.
3. Khudair SF, Alshammari HN, Alkhafaji HAAR. Association of Peripheral Blood Parameters With TNM Stage of Breast Cancer. Hilla University College Journal for Medical Science. 2024;2(2):15–19.
4. Miller KD, *et al.* Cancer treatment and survivorship statistics, 2019. CA: a cancer journal for clinicians. 2019;69(5):363–385.
5. Valencia OM, *et al.* The role of genetic testing in patients with breast cancer: A review. JAMA surgery. 2017;152(6):589–594
6. Abrahams HJG, *et al.* Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: A meta-analysis involving 12 327 breast cancer survivors. Annals of Oncology. 2016;27(6):965–974.
7. Yaman M, Kaya G, Yekeler H. Distribution of trace metal concentrations in paired cancerous and non-cancerous human stomach tissues. World Journal of Gastroenterology: WJG. 2007;13(4):612.
8. Schrauzer GN. Effects of selenium and low levels of lead on mammary tumor development and growth in MMTV-infected female mice. Biological trace element research. 2008;125(3):268–275.
9. Samson KLI, Fischer JAJ, Roche ML. Iron status, anemia, and iron interventions and their associations with cognitive and academic performance in adolescents: A systematic review. Nutrients. 2022;14(1):224.
10. Marques, O, *et al.* Iron homeostasis in breast cancer. Cancer letters. 2014;347(1):1–14.
11. BO A, *et al.* Selenoprotein synthesis: An expansion of the genetic code. Trends in biochemical sciences. 1991;16:463–467.
12. Gerber M, *et al.* Oxidant-antioxidant status alterations in cancer patients: Relationship to tumor progression. The Journal of nutrition. 1996;126:1201S–1207S.
13. Lopez-Saez JB, Senra-Varela A, Pousa-Estevez L. Selenium in breast cancer. Oncology. 2003;64(3):227–231.
14. Ramadhan HH, Mohammed RN. Biomarkers and the identification of kidney damage in patients with diabetes mellitus. Hilla University College Journal For Medical Science. 2024;2(4):41–51.
15. Nuttall FQ. Body mass index: obesity, BMI, and health: a critical review. Nutrition today. 2015;50(3):117–128.
16. Sharma P, Reddy PK, Kumar B. Trace element zinc, a nature's gift to fight unprecedented global pandemic COVID-19. Biological trace element research. 2021;199(9):3213–3221.
17. Cabral M, *et al.* Trace element profile and incidence of type 2 diabetes, cardiovascular disease and colorectal cancer: results from the EPIC-Potsdam cohort study. European journal of nutrition. 2021;60(6):3267–3278.
18. Mears J, Treacy M. Body fluids and electrolytes. In: Acute Nursing Care. Routledge, 2020. p. 97–134.
19. Robey IF, *et al.* Bicarbonate increases tumor pH and inhibits spontaneous metastases. Cancer research, 2020;69(6):2260–2268.
20. Ahmed F, Mohammed A. Magnesium: the forgotten electrolyte—A review on hypomagnesemia. Medical Sciences. 2019;7(4):56.
21. Dibaba D, *et al.* Magnesium intake and incidence of pancreatic cancer: The vitamins and lifestyle study. British journal of cancer. 2015;113(11):1615–1621.
22. Halaby R, Abdollahi J, Martinez ML. Acid phosphatase activity in human breast tumors. Breast Cancer Research. 2001;3(2):E002.
23. Gałęska E, *et al.* Reproductive consequences of electrolyte disturbances in domestic animals. Biology. 2022;11(7):1006.
24. Ferreira JP, *et al.* Abnormalities of potassium in heart failure: JACC state-of-the-art review. Journal of the American College of Cardiology. 2020;75(22):2836–2850.
25. Torti SV, *et al.* Iron and cancer. Annual review of nutrition. 2018;38(1):97–125.
26. Galaris D, Pantopoulos K. Oxidative stress and iron homeostasis: mechanistic and health aspects. Critical reviews in clinical laboratory sciences. 2008;45(1):1–23.
27. Guo W, *et al.* An important role of the hepcidin–ferroportin signaling in affecting tumor growth and metastasis. Acta biochimica et biophysica Sinica. 2015;47(9):703–715.
28. Lappano R, *et al.* Recent advances on the stimulatory effects of metals in breast cancer. Molecular and cellular endocrinology. 2017;457:49–56.
29. Lamy PJ, Durigova A, Jacot W. Iron homeostasis and anemia markers in early breast cancer. Clinica chimica acta. 2014;434:34–40.
30. F Jr. CG. Current evidence and research needs to support a health claim for selenium and cancer prevention. The Journal of Nutrition. 2005;135(2):343–347.
31. Zakharia Y, Bhattacharya A, Rustum YM. Selenium targets resistance biomarkers enhancing efficacy while reducing toxicity of anti-cancer drugs: Preclinical and clinical development. Oncotarget. 2018;9(12):10765.
32. Vinceti M, *et al.* Selenium for preventing cancer. Cochrane database of systematic reviews. 2018;1.
33. Choi R, *et al.* Serum trace elements and their associations with breast cancer subgroups in Korean breast cancer patients. Nutrients. 2018;11(1):37.
34. Lubinski J, *et al.* Serum selenium levels predict survival after breast cancer. Breast cancer research and treatment. 2018;167(2):591–598.
35. Khraibet MR, Kadhim EJ. Anti-lung cancer activity of the herbal medicinal plant cycas revoluta. Hilla University College Journal For Medical Science. 2025;3(2):25–30.