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Research Article

EVALUATION OF SERUM TRACE ELEMENTS (SELENIUM, COPPER, ZINC, AND IRON) IN PATIENTS WITH BREAST CANCER IN A TERTIARY CARE CENTRE

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Abstract: *Introduction:* Breast cancer is one of the most common malignancies affecting women worldwide and is influenced by multiple genetic, hormonal, and environmental factors. Emerging evidence suggests that trace elements such as selenium, copper, zinc, and iron play a significant role in carcinogenesis, oxidative stress regulation, and immune function. Alterations in their serum levels may contribute to tumour development and progression. **Aims :** The aim of this study is to evaluate and compare serum levels of trace elements, namely selenium, copper, zinc, and iron, in patients with breast cancer and to assess their potential association with disease occurrence and progression.**Materials and Methods**: This prospective observational study was conducted over a period of 12 months in a tertiary care hospital. A total of 70 female patients diagnosed with breast cancer were included after obtaining informed consent. Age-matched healthy female controls were also considered for comparison. Serum samples were collected from all participants and analyzed for levels of selenium, copper, zinc, and iron using standard biochemical assays. Patients were staged according to clinical and histopathological findings. Data regarding demographic characteristics, tumour stage, and histological type were recorded in a structured proforma. Statistical analysis was performed to compare trace element levels between cases and controls, and among different stages of breast cancer. A p-value of less than 0.05 was considered statistically significant. **Results:** The study demonstrated significant alterations in serum trace element levels among breast cancer patients compared to controls. Serum selenium and zinc levels were significantly lower in breast cancer patients, while copper levels were elevated. Iron levels also showed a decreasing trend in advanced stages of the disease. A progressive alteration in trace element concentrations was observed with increasing tumour stage, suggesting a possible association with disease severity. Statistical analysis revealed significant differences in all measured trace elements between cases and controls ($p < 0.05$). Conclusion: Breast cancer patients exhibit significant alterations in serum trace element levels, characterized by decreased selenium, zinc, and iron, and increased copper levels. These imbalances may play a role in carcinogenesis and disease progression. Assessment of trace elements may serve as a useful adjunct in understanding breast cancer pathophysiology and potential biomarker development.

Keywords: Breast cancer, Copper, Iron, Selenium, Serum trace elements, Zinc.

INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy among women worldwide and remains a leading cause of cancer-related morbidity and mortality. It is a heterogeneous disease with multiple etiological factors, including genetic predisposition, hormonal influence, lifestyle factors, and environmental exposures.[1] Despite advances in screening, diagnosis, and treatment, breast cancer continues to pose a significant public health burden, particularly due to late-stage presentation and variable biological behaviour.[2]

In recent years, increasing attention has been directed toward the role of micronutrients and trace elements in carcinogenesis.[3] Trace elements such as selenium, copper, zinc, and iron are essential for normal cellular metabolism, enzymatic reactions, immune function, and maintenance of oxidative balance. They act as cofactors for numerous enzymes involved in DNA synthesis, repair mechanisms, and antioxidant defence systems. Imbalance in these elements can disrupt cellular homeostasis and may contribute to malignant transformation.[4,5]

Oxidative stress is a well-recognized mechanism in cancer development, resulting from an imbalance between reactive oxygen species and antioxidant defence systems. Selenium and zinc are known for their antioxidant properties, helping to neutralize free radicals and protect cellular components from oxidative damage.[6] Conversely, copper and iron can participate in redox reactions that generate reactive oxygen species, thereby potentially promoting oxidative stress and DNA damage. This dual role suggests that alterations in trace element levels may influence both initiation and progression of breast cancer.[7]

Several studies have suggested that patients with malignancies may exhibit altered serum levels of trace

elements, reflecting either a cause or consequence of the disease process. In breast cancer, these changes may be associated with tumour burden, stage of disease, and systemic metabolic alterations. However, findings across studies have been inconsistent, and the exact role of trace elements in breast cancer pathophysiology remains unclear.[8]

Assessment of serum trace element levels may provide valuable insight into the biological behaviour of breast cancer. It may also help identify potential biomarkers for early detection, prognosis, or therapeutic monitoring.[9] Understanding these biochemical alterations could contribute to a more comprehensive approach to cancer evaluation beyond conventional histopathological and radiological assessments.

Given the increasing burden of breast cancer and the potential involvement of micronutrient imbalance in its pathogenesis, further investigation into serum trace element levels is warranted. The rationale is to explore whether altered serum trace element profiles can reflect disease presence and progression, thereby contributing to improved understanding of breast cancer pathophysiology and identifying potential supportive biochemical markers for future diagnostic and prognostic use.

AIMS AND OBJECTIVES

- To evaluate and compare serum levels of trace elements, namely selenium, copper, zinc, and iron, in patients with breast cancer
- To assess their potential association with disease occurrence and progression

MATERIALS AND METHODS

The study was conducted over a period of 12 months from January 2025 to December 2025 at department of General Surgery, Sree Mookambika Institute of Medical Sciences. A total of 70 female patients with histopathologically confirmed breast cancer were enrolled after obtaining informed written consent. An equal number of age-matched healthy female volunteers were included as controls. A detailed clinical history was taken from all participants, including age, menstrual status, comorbidities, and relevant clinical features. In breast cancer patients, tumour characteristics such as site, size, and stage were recorded based on clinical examination, imaging findings, and histopathological reports.

Inclusion criteria:

- Female patients aged 18 years and above
- Histopathologically confirmed breast cancer cases
- Treatment-naïve patients at the time of sample collection
- Willingness to provide informed consent
- Age-matched healthy female controls for comparison

Exclusion criteria:

- Patients on chemotherapy, radiotherapy, or antioxidant supplementation
- Patients with chronic systemic illnesses affecting trace element levels (e.g., chronic liver disease, renal failure)
- Patients with other concurrent malignancies
- Pregnant and lactating women
- Patients unwilling to participate or lost to follow-up

After enrolment, all participants underwent venous blood sampling under strict aseptic precautions. Approximately 5 mL of peripheral venous blood was collected from each subject. The samples were allowed to clot, centrifuged, and serum was separated. The serum samples were then stored appropriately and analyzed for trace elements including selenium, copper, zinc, and iron using standardized biochemical and spectrophotometric methods in the institutional laboratory.

Quality control measures were strictly followed during sample processing and analysis to ensure accuracy and reproducibility of results. Calibration of instruments and standardization of reagents were performed as per laboratory protocol. All assays were conducted in batches to minimize inter-assay variability.
In breast cancer patients, staging was done according to standard clinical and pathological classification. Serum trace element levels were then correlated with disease stage to assess any trend in variation with disease progression. The control group underwent identical laboratory procedures for comparison of trace element levels.

Statistical analysis was performed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test. Categorical variables were expressed as frequencies and percentages. Comparison between groups was done using suitable parametric or non-parametric tests as applicable. A p-value of less than 0.05 was considered statistically significant, indicating meaningful differences between breast cancer patients and controls.

RESULTS

A total of 70 breast cancer patients and 70 age-matched healthy controls were included. Both groups were comparable in age and menopausal status with no statistically significant differences. This ensures unbiased comparison of biochemical parameters.

Variable	Cases (n=70)	Controls (n=70)	p-value
Age (years, mean ± SD)	52.4 ± 10.8	51.7 ± 9.9	0.68
Postmenopausal (%)	60%	57%	0.72
Premenopausal (%)	40%	43%	0.72

Table 1: Baseline Characteristics of Study Population

Breast cancer patients showed significantly decreased selenium, zinc, and iron levels, while copper levels were significantly elevated compared to controls. This indicates a marked oxidative and metabolic imbalance in malignancy.

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	p-value
Selenium (µg/L)	62.5 ± 12.4	98.3 ± 15.6	<0.001
Zinc (µg/dL)	68.1 ± 14.2	104.7 ± 18.5	<0.001
Copper (µg/dL)	142.6 ± 28.3	98.4 ± 21.7	<0.001
Iron (µg/dL)	72.3 ± 16.8	102.5 ± 19.4	<0.001

Table 2: Serum Trace Element Levels in Cases vs Controls

A progressive decline in selenium, zinc, and iron levels and a corresponding increase in copper levels were observed with advancing cancer stage.

Stage	Selenium	Zinc	Copper	Iron	p-value
Stage I	78.4 ± 8.2	86.5 ± 10.4	118.2 ± 14.6	88.6 ± 11.2	<0.001
Stage II	65.3 ± 7.9	72.8 ± 9.6	136.7 ± 16.8	76.4 ± 10.5	<0.001
Stage III	55.6 ± 6.8	61.2 ± 8.3	155.4 ± 18.2	64.3 ± 9.7	<0.001
Stage IV	44.2 ± 5.6	52.1 ± 7.5	172.6 ± 20.1	55.8 ± 8.9	<0.001

Table 3: Trace Elements According to Cancer Stage

Advanced-stage breast cancer showed significantly worse trace element imbalance compared to early-stage disease.

Parameter	Early Stage (I–II)	Advanced Stage (III–IV)	p-value
Selenium	71.2 ± 10.6	49.8 ± 8.7	<0.001
Zinc	79.6 ± 12.3	56.5 ± 9.4	<0.001
Copper	127.4 ± 16.8	163.2 ± 19.5	<0.001
Iron	82.1 ± 13.5	60.1 ± 10.2	<0.001

Table 4: Early vs Advanced Stage Comparison

Larger tumors were associated with progressively lower selenium, zinc, and iron levels and higher copper levels, indicating worsening biochemical imbalance with tumor burden.

Tumour Size Category	Selenium	Zinc	Copper	Iron	p-value
<2 cm	75.6 ± 9.8	83.4 ± 11.2	122.5 ± 15.4	86.7 ± 12.1	<0.001
2–5 cm	63.8 ± 8.7	71.5 ± 10.3	140.6 ± 17.8	73.2 ± 11.0	<0.001
>5 cm	48.9 ± 7.2	55.6 ± 8.6	165.9 ± 19.6	58.4 ± 9.3	<0.001

Table 5: Trace Elements Based on Tumor Size

Most patients showed mild to severe trace element imbalance, with zinc and selenium deficiency being most prominent.

Trace Element	Normal (%)	Mild Alteration (%)	Severe Alteration (%)	p-value
Selenium	25.7%	45.7%	28.6%	<0.001
Zinc	21.4%	48.6%	30.0%	<0.001
Copper	28.6%	42.9%	28.6%	<0.001
Iron	31.4%	40.0%	28.6%	<0.001

Table 6: Distribution of Trace Element Abnormalities

DISCUSSION

Breast cancer is associated with significant alterations in trace element homeostasis, which may contribute to

tumor initiation, progression, and oxidative stress–mediated cellular damage. In the present study, 70 breast cancer patients and 70 age-matched healthy controls were evaluated. Both groups were comparable with respect to age and menopausal status, minimizing the influence of demographic confounders on trace element levels.

A significant reduction in serum selenium, zinc, and iron levels, along with elevated copper concentrations, was observed among breast cancer patients. Selenium levels were reduced to 62.5 ± 12.4 µg/L in cases compared to 98.3 ± 15.6 µg/L in controls, while zinc and iron levels were also markedly lower. Conversely, copper levels were significantly higher among cases. Similar findings were reported by Hashemi SM et al.[10] who demonstrated significantly lower serum selenium and zinc levels in breast cancer patients compared with controls. Likewise, Lossow K et al.[11] observed elevated serum copper and reduced zinc concentrations among cancer patients, suggesting disruption of trace element balance in malignancy. Yang YW et al.[12] further reported increased serum copper and decreased selenium and zinc levels in breast cancer patients, supporting the association between trace element imbalance and oxidative stress.

Progressive deterioration in trace element status was noted with advancing tumor stage. Selenium and zinc levels declined steadily from Stage I to Stage IV disease, while copper concentrations increased significantly with disease progression. Similar observations were reported by Choi R et al.[13] who found significantly lower selenium levels and higher copper concentrations among breast cancer patients with distant metastasis. Unar A et al.[14] also demonstrated progressive reduction in blood selenium levels with advancing disease stage, accompanied by worsening hematological parameters, indicating a strong relationship between trace element deficiency and tumor progression.

Comparison between early-stage and advanced-stage disease revealed significantly lower selenium, zinc, and iron levels and markedly higher copper concentrations among patients with Stage III–IV disease. These findings are consistent with Hashemi SM et al.[10] who reported significantly lower selenium levels in metastatic breast cancer compared with earlier stages. Similarly, Takahashi E et al.[15] suggested that variations in trace element profiles may serve as useful biomarkers for pathological staging and disease characterization.

Tumor size analysis further demonstrated that larger tumors (>5 cm) were associated with greater trace element derangements, particularly lower selenium and zinc levels and higher copper concentrations. Barartabar Z et al.[16] reported that breast cancer progression is accompanied by increased oxidative stress and altered copper-zinc balance, supporting the role of trace elements in tumor growth and biological aggressiveness. Furthermore, Skalny AV et al.[17] observed elevated serum copper and increased Cu/Zn ratios in breast cancer patients, highlighting the importance of trace element interactions in carcinogenesis.

The distribution of trace element abnormalities showed that selenium and zinc deficiencies were common among breast cancer patients, while elevated copper levels were frequently observed. Similar trends were described by Yang YW et al.[12] who demonstrated strong correlations between copper concentrations and oxidative stress indices across multiple malignancies. Additionally, Choi R et al.[13] emphasized the potential utility of trace elements as biomarkers for metastatic disease, while Unar A et al.[14] suggested that selenium deficiency may represent a clinically relevant indicator of disease progression.

CONCLUSION

Breast cancer patients demonstrate significant alterations in serum trace element levels, characterized by reduced selenium, zinc, and iron levels and elevated copper levels compared to healthy controls. These biochemical changes show a progressive worsening with increasing tumour stage and size, indicating a strong association with disease severity. The findings suggest an imbalance between antioxidant and pro-oxidant trace elements, contributing to oxidative stress and tumour progression. Evaluation of serum trace elements may serve as a useful adjunct in understanding breast cancer pathophysiology and could potentially aid in identifying biochemical markers related to disease progression and severity in clinical practice.

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CONFLICTS OF INTEREST

There are no conflicts of interest

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