ONLINE FIRST

ORIGINAL ARTICLE

Serum Metals in Breast Cancer Patients: A comparative study conducted at Hyderabad and its Adjoining Areas, Pakistan

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doi: 10.22442/jlumhs.2025.01264

ABSTRACT

OBJECTIVE: This study aims to measure the concentrations of various metals in the blood serum of breast cancer patients from Hyderabad and surrounding areas and compare them with healthy controls.

METHODOLOGY: This comparative case-control study was conducted at the Institute of Biochemistry, University of Sindh, Jamshoro. Samples were collected from the surgical wards at Liaquat University of Medical & Health Sciences. The study included 518 participants, including 259 newly diagnosed breast cancer patients with a mean age of 51.10±7.761 and no prior radio or chemotherapy treatment. Patients who had previous breast surgery were excluded. The study also included 259 age-matched healthy controls without a history of cancer. After obtaining the participants' sociodemographic characteristics, blood samples were collected and analyzed for serum metal concentrations using inductively coupled plasma optical emission spectrometry (ICP-OES). Data was analyzed by SPSS version 20.0, $p < 0.05$ is considered a significance level at a 95% confidence interval.

RESULTS: We found the majority of the breast cancer patients were less than 50 years of Age, illiterate, and belonged to Hyderabad district and Punjabi by ethnicity. The results revealed significant differences in metal concentrations between breast cancer patients and controls, with elevated levels of metals such as aluminum, cobalt, chromium, and lead. At the same time, elements like arsenic and zinc were lower in breast cancer patients.

CONCLUSION: The findings suggest that the serum metal concentration may be linked to breast cancer pathogenesis, highlighting the need for further research on environmental risk factors in breast cancer progression.

KEYWORDS: Breast cancer, serum metals, atomic absorption spectrophotometry, Inductive coupled plasma (ICP), biological processes, Sociodemographic factors.

INTRODUCTION

Trillions of cells make up the human body; during a person's lifetime, these cells normally develop, divide, and die naturally[1]. Breast cancer is a proliferative illness of the breast tissue and is the most frequent cancer among women. In Asia, Pakistan has the highest rate of breast cancer, with 1 in every nine women[2]. Inadequate knowledge, lack of awareness, ignorance and illiteracy are the main reasons for late breast cancer detection. Breast cancer could be easier to diagnose and manage if women have proper knowledge of breast cancer, as reported by the Breast Health Global Initiative (BHGI)[3]. Ethnicity: Patients without adequate education about their employment position, income, and education are linked to disease[4]. Multiple factors contribute to delayed presentation, including lack of awareness, cultural inhibitions, poverty, and fear of disease outcomes[5]. Environmental contamination directly impacts human health, which depletes natural resources and generates enormous amounts of trash. Acid rain, global warming, and the release of heavy metals contaminating air, water, land, and oceans are among the global problems caused by this waste[6]. Heavy metals are dangerous substances with a high density that we are exposed to by ingestion or inhalation. Living or working close to industrial sites or away from those sites (especially metal contaminants in water) exposes one to these metals, and diseases may arise as a result of inadequately disposed of metal sites[7]. The study aimed to quantify the levels of various metals in the blood serum of patients in comparison to controls and use correlation analysis to look at the correlations between the metal levels.

METHODOLOGY

The case-control study was conducted at the Institute of Biochemistry, Faculty of Natural Sciences, University of Sindh, Jamshoro, Sindh, Pakistan. In contrast, the sample collection was done from the surgical wards at Liaquat University of Medical & Health Sciences. A total of 518 participants were included in the study, among them 259 newly diagnosed breast cancer patients with a mean age of 51.10 ± 7.761 and 259 age-matched controls with adverse personal and family history of cancer lesions. Before including them in the study, each participant signed informed written consent, and the Department of Biochemistry, University of Sindh, Institutional Ethics Committee, via letter No. IOB/244/2023, approved the study procedure. Participants food habits, personal and family histories, and sociodemographic traits were all covered via a standardized questionnaire used to collect data. About 5ml of Blood was collected via venepuncture in serum tubes from participants to analyze serum metals. Samples were prepared using the reported conventional wet acid digestion (CADM) method[8], and serum metal levels were determined using an inductively coupled plasma optical emission spectrometer (ICP-OES). SPSS version 20.0 was used for data analysis to compare serum metal levels across various demographic categories between patients and controls. The mean ± SD is used to express the values. The student's 't' test was used to compare the two groups, and the analysis of variance (ANOVA) test was used to compare the groups. The 95% confidence interval showed that less than 0.05 P-value was considered statistically significant.

RESULTS

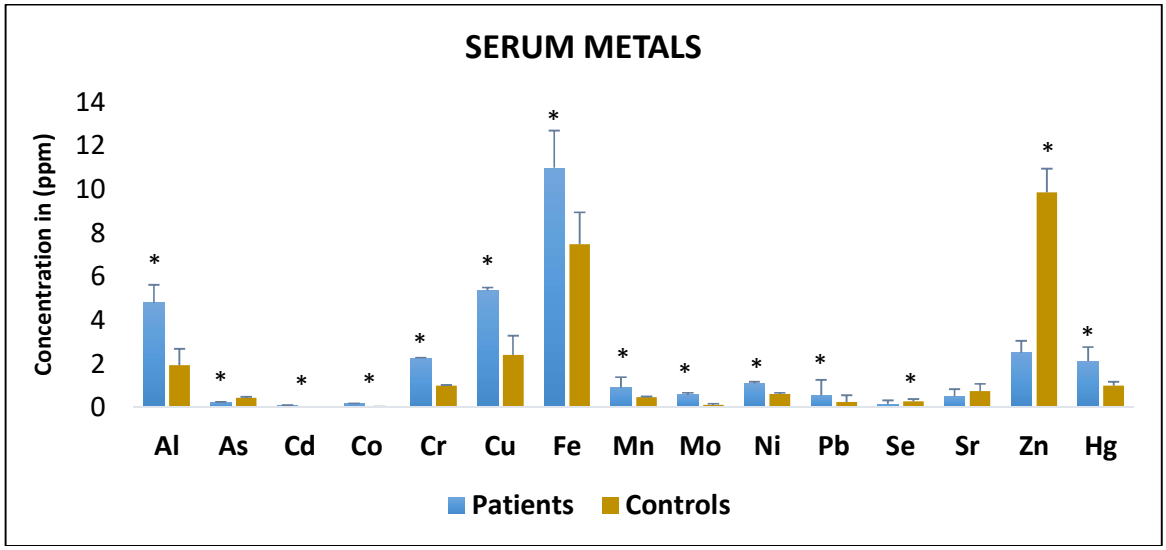
Table I shows the breast cancer patients and controls' general sociodemographic characteristics. Among the 259 breast cancer patients, the mean age of breast cancer patients and control was 51.26±7.753 and 49.06±7.516 years, respectively. It was found that most of the breast cancer patients were married, illiterate and belonged to Hyderabad district, and Punjabi by ethnicity. Moreover, the breast cancer patients had no family history of breast cancer. Unemployment (96.7% housewives) and a history of obesity were evident in breast cancer patients and those with a physically active lifestyle. The majority of the breast cancer patients had no psychological problems discouraging smoking, addiction to anything and Unani medicines intake. We found that most breast cancer patients consumed chicken (white meat) and surface water for drinking compared to control subjects. There is a comparison of percentages of participants who were married and breastfed their babies with those who were single /unmarried. We found that the majority (86.7%) of breast cancer were married and fed their babies properly (≥ 2 years). Our study revealed that breast cancer patients with normal skin complexion (61.4%) were more affected by the pathogenesis of breast cancer.

Table I: General sociodemographic characteristics of the study participants

	Patients (n=259) %	Controls (n=259) %		Patients (n=259) %	Controls (n=259) %
Mean Age (years)	51.26±7.753	49.06±7.516	**Occupation**		
Marital status			House Wife	96.7	40.0
Married	93.30	80.0	Employed	3.3	60.0
Unmarried	6.70	20.0	**Obesity in past**		
Ethnicity			Yes	60	46.7
Balochi	5.40	44.80	No	40	53.3
Muhajir	4.60	9.80	**Family History**		
Pathan	5.40	2.00	Positive	20.0	0
Punjabi	66.0	5.90	Negative	80.0	100.0
Sindhi	16.60	78.40	**Life style**		
District			Physically active	100	86.7
Badin	5.4	0	Sedentary	0	13.30
Bhitshah	4.6	4.2	**Unani medicines**		
Dadu	5.3	0.0	Yes	3.30	0
Hyderabad	66.0	67.2	No	96.70	**0**
Jamshoro	16.8	18.9	**Smoking status**		
Tando Allahyar	1.9	1.9	Smoker	10	0
Sanghar	0.0	3.2	Non-smoker	90	100
Education			**Addiction**		
Uneducated	68.30	45.20	Addictive	26.60	43.30
Primary	12.70	10.40	Non- Addictive	73.40	56.70
Matriculation	15.10	5.40	**Drinking water**		
Intermediate	3.90	1.90	Surface water	51.70	59.80
Graduation	0	9.30	Underground water	48.30	40.20
Masters	0	27.8	**Breast Feeding**		
Type of meat			Yes	78.80	66.80
White	95.40	44.40	No	5.0	10.0
Red	4.60	15.80	Unmarried	16.2.0	23.20
Both	0	39.80			
Psychological problem			**Color Complexion**		
Stress	40.0	60.0	Fair	27.8	30.1
Anxiety	0	10.0	Normal	61.4	66.4
No any	60.0	30.0	Dark	10.8	3.5

Figure I compared the concentrations of serum metals between breast cancer patients (n=259) and healthy controls (n=259). The concentration of Al is significantly higher in patients compared to controls. Similarly, Co, Cr, Cu, Fe, Mn, Mo, Ni, Pb, and Hg levels are also elevated in patients compared to controls, with p-values ranging from 0.000 to 0.039, indicating strong statistical significance. In contrast, elements such as As, Se and Zn showed significantly lower concentrations in the breast cancer patients than in controls. These findings suggested a distinct variation in trace element profiles between breast cancer patients and healthy controls, which could have implications for the role of these elements in cancer progression or susceptibility.

Figure I: Comparison of serum metals between breast cancer patients and control



The data presented in **Table II** compared serum metal concentrations among breast cancer patients, categorized by marital status, menopausal status, and breastfeeding status.
Certain metals showed statistically significant variations based on marital, menopausal, and breastfeeding status. For instance, Fe was significantly higher in unmarried women than married ones ($p<0.05$). Similarly, Mn and Zn levels were significantly higher in post-menopausal women compared to pre-menopausal women ($p<0.05$). Regarding breastfeeding status, As, Pb and Mn levels were considerably higher in breastfeeding women than those who did not breastfeed ($p<0.05$). The findings suggested that exposure to or metabolism of these metals is affected by hormonal or physiological changes associated with these factors.

Table I: Comparison of serum metals between marital, Menopausal and breastfeeding status of breast cancer patients

Serum Metal (ppm)	Married Mean ± SD	Unmarried Mean ± SD	Menopause Mean ± SD	Pre-menopause Mean ± SD	Breastfeeding Mean ± SD	No breastfeeding Mean ± SD
Al	5.026±2.973	3.405±1.171	4.985±3.248	4.320±1.286	3.405±1.171	5.177±3.030
As	0.247±0.245	0.188±0.043	0.251±0.263	0.205±0.096	3.006±0.114¶	0.188±0.043
Cd	0.085±0.155	0.055±0.032	0.094±0.169	0.045±0.023	0.226±0.186	0.518±0.684
Co	0.166±0.232	0.172±0.155	0.128±0.134	0.265±0.351	0.055±0.032	0.086±0.161
Cr	2.215±1.249	2.498±1.546	2.167±1.128	2.480±1.636	0.062±0.041	0.172±0.155
Cu	4.923±5.035	8.046±5.246	4.850±4.233	6.672±6.949	0.169±0.239	0.124±0.127
Fe	10.90±5.922	11.49±4.506*	10.60±3.912	11.96±8.955	2.498±1.546	2.283±1.253
Mn	0.947±1.575*	0.756±0.259	0.973±1.710#	0.786±0.408	1.312±0.890	8.046±5.246
Mo	0.601±0.962	0.416±0.236	0.539±0.841	0.670±1.056	5.238±5.076	0.721±1.193
Ni	1.096±0.833	1.067±0.521	1.088±0.873	1.101±0.564	11.49±4.506	11.10±6.091
Pb	0.539±0.738	0.620±0.594	0.540±0.775	0.577±0.556	8.232±1.229¶	0.756±0.259
Se	0.157±0.178	0.155±0.068	0.147±0.149	0.182±0.210	0.994±1.625	0.327±0.089
Sr	0.498±0.348	0.556±0.187	0.509±0.358	0.499±0.255	0.416±0.236	0.467±0.719
Zn	2.610±2.710	1.982±0.750	2.774±2.777#	1.876±1.665	2.391±2.048	1.067±0.521
Hg	2.167 ± 1.842	1.897±0.866	2.247±1.762	1.827±1.687	0.998±0.613	2.404±2.119

**p<0.05 when married compared with unmarried.*
 # p<0.05 when menopausal compared with pre-menopausal women.
¶ p<0.05 when breastfeeding women compared with No breastfeeding.

DISCUSSION

The mean Age of the 54 female breast cancer patients and the 54 female controls in the study was 47.2±8.14 years and 46.8±8.4 years, respectively[9]. Another study conducted on 287 Korean female subjects participated, and the (interquartile range) ages were 48.0 years (43.0–56.0 years) for controls and 46.0 years (40.0–53.0) for patients, respectively[10]. These studies are relevant to the present study, where our study population comprises 259 breast cancer patients with a mean age of 51.26±7.753 years **(Table I).** In a study conducted on 200 patients with breast carcinoma, out of them, 94 females were migrants (47%), 39 were non-migrants (19%), 25 were Punjabi (12.0%), 13 were Pathan (7.0%), 7 were Baloch (4.0%), and 22 (11.0%) belonged to minority ethnic groups[11]. Whereas our findings are quite different, Punjabi women (66.0%) are more affected by breast cancers. The ethnic variation could also be due to different genetics[12]. A factor identified in other studies shows regression analysis as significant in having a pertinent family history, i.e. mother, grandmother, sister or a cousin sister had breast cancer as well[13]. In contrast, our study does not coincide with this fact. A total of 80% of breast cancer patients included in our study have an adverse family history of this ailment. Our findings suggest that unemployment (96.7% of housewives) was obvious in breast cancer patients. In contrast, a study found no significant association between employment and breast cancer [(14)]. Another observational study reported the prevalence of obesity at 46.6% in Pakistani breast cancer patients and analyzed the relationship of BMI with menopausal status and other prognostic factors [(15)]. In the current study, the prevalence of a history of obesity was suggestive amongst the breast cancer population. Lack of physical activity status was found to have significant positive associations with breast cancer[16]. It was revealed from our study that the majority of breast cancer patients were physically active and preferred to work at their houses. Marital status of unmarried (OR2.03; 95%CI, 1.69-2.44), lack of breastfeeding, smoking (current or ever), lack of physical activity and post-menopausal status were found to have significant positive associations with breast cancer. It was also observed that increased parity reduced the disease risk[16].

Another study found that people with breast cancer had reduced levels of zinc (Zn), which could be a factor in the disease's progression. Zinc levels varied, contributing to both elevated and lowered levels. Iron and zinc levels in beef dropped in the patient group consuming beef and chicken, and these findings were linked to the advancement of breast cancer. To lower the incidence of breast cancer, increase early detection efforts and keep an eye on milk and water levels of heavy metals in milk and water, especially iron and zinc, to limit environmental risks[17]. Another study found that the biological samples of female patients with breast cancer had decreased levels of zinc. Compared to non-cancerous participants, female breast cancer patients had a higher observed result of hazardous elements (Cd).

A recent analytical study suggested the mean concentration of lead (Pb) observed was higher than the normal control[18]. It has been discovered that serum levels of lead (Pb) are statistically considerably higher. The effects of heavy metals, Pb, Ni, and Cd, were assessed in the Blood of patients with breast cancer. Statistically high concentrations of these metals were found in patients aged 25 to 60 years compared to controls, indicating the need for effective legislation and identifying areas with higher levels of heavy metals, as failure to do so may lead to serious complications down the road[19]. Serum trace element levels in 88 patients and 84 controls are compared in another investigation. Serum levels of Mn, Al, and Fe were considerably lower in breast cancer patients than in controls, but those of Cd, Cu, Co, and Cr were significantly higher

and borderline high. However, there were no significant differences in serum levels of Zn, Pb, Se and Ni between the two groups[20].
A study done in 2023 emphasized heavy metals, specifically Cu, Cd, Zn, Mn, Pb, and Ni, can cause the development of breast cancer. Hence, early detection of breast cancer may be helped by heavy metal level measurement. Raised levels of Cu and Cd and lower levels of Zn and Mn may contribute to this ailment's pathogenesis[21]. These findings suggest a distinct variation in metal profiles between breast cancer patients and healthy individuals, which could have implications for the role of these elements in cancer progression or susceptibility.

CONCLUSION

This study reveals significant differences in serum metal concentrations between breast cancer patients and controls, suggesting heavy metal exposure plays a role in the pathogenesis of breast cancer. Elevated levels of metals like aluminum, cobalt, chromium, and lead in patients point to environmental pollutants as potential contributors, while lower zinc levels hint at imbalances in essential trace elements. These findings emphasize the need to monitor the exposure of metals and call for further research to confirm a link between metal exposure and breast cancer, as well as preventive measures that may also be taken into consideration.

Ethical permission: Department of Biochemistry, University of Sindh, Jamshoro, IRB letter No. IOB/244/2023.
Conflict of Interest: No conflicts of interest, as stated by authors.
Financial Disclosure / Grant Approval: Authors did not receive any funding from any source, research was carried out through facilities provided by the Institute of Biochemistry, University of Sindh, Jamshoro.
Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Laghari M: Designed the study, analyzed the data using statistical tools, drafted the manuscript.
Channa NA: Designed the study, drafted the manuscript, supervised.
Shaikh M: Collected the data, compiled the data, analyzed the data using statistical tools, reviewed and edited the manuscript.
Hameed S: Collected the data, drafted the manuscript.
Mumtaz N: Collected the data, compiled the data.
Hameed Z: Compiled the data, reviewed and edited the manuscript.
All authors read and approved the final manuscript.

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