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COMPARISON OF SERUM IRON, ZINC, AND SELENIUM LEVELS BETWEEN PREMENOPAUSAL AND POSTMENOPAUSAL WOMEN IN THE SOUTH INDIAN POPULATION: A DESCRIPTIVE STUDY

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ABSTRACT

Background: Menopause is a crucial physiological transition in women, leading to biochemical and metabolic changes, particularly affecting trace element metabolism. Iron (Fe), zinc (Zn), and selenium (Se) are essential micronutrients involved in enzymatic antioxidant defense, immune regulation, and bone metabolism. However, data on their variations in postmenopausal women, especially in the South Indian population, remains limited. **Objective:** This study aimed to compare serum Fe, Zn, and Se levels between premenopausal and postmenopausal women and assess their variations with advancing postmenopausal age in a South Indian population.

Materials and Methods: A cross-sectional study was conducted over nine months (January–September 2024) at a tertiary care center in Hyderabad, Telangana, India. A total of 200 women, comprising 100 premenopausal (30–45 years) and 100 postmenopausal (46–75 years) participants, were recruited. Postmenopausal women were defined as those with amenorrhea for at least one year and not on hormone replacement therapy (HRT) or other menopause-related treatments for at least six months. Blood samples were collected via venipuncture, and serum Fe, Zn, and Se levels were measured using ELISA-based and spectrophotometry-based assays. Data were analyzed using Student's t-test, with $p < 0.05$ considered statistically significant.

Results: No statistically significant differences in Fe, Zn, and Se levels were observed between premenopausal and postmenopausal women. However, trends with advancing postmenopausal age were noted. Serum Fe levels progressively increased with age, except for a transient decline in the 56–60 years group, suggesting potential Fe accumulation in older women. Serum Zn levels significantly increased after 61 years, likely due to bone resorption and metabolic adaptations. Conversely, serum Se levels consistently declined with age, indicating a potential deficiency risk that may contribute to increased oxidative stress and associated health complications.

Conclusion: Although no significant menopausal differences were observed in Fe, Zn, and Se levels, age-related fluctuations suggest the need for regular nutritional monitoring and dietary interventions. Increased Fe levels in older postmenopausal women necessitate routine Fe monitoring to prevent oxidative damage, while Zn supplementation may support bone and immune health. The declining Se levels highlight the need for increased dietary intake through Se-rich foods such as seafood and Brazil nuts to counteract oxidative stress. Encouraging physical activity can also help regulate metabolism and

micronutrient utilization. These findings emphasize the importance of targeted nutritional strategies to mitigate menopause-related oxidative stress and health risks in South Indian postmenopausal women.
Keywords: Menopause, Iron (Fe), Zinc (Zn), Selenium (Se), Postmenopausal Women, Oxidative Stress, Nutritional Monitoring, Micronutrient Deficiency, Bone Metabolism, Hyderabad, South Indian Population.

INTRODUCTION

Menopause is an inevitable physiological transition in women, marked by the permanent cessation of ovarian functions, including ovulation and hormonal secretion. This transition significantly impacts multiple metabolic pathways, leading to physiological and biochemical alterations that often impair the quality of life.[1,2] The hormonal decline, particularly in estrogen levels, contributes to various metabolic disturbances, including dysregulated lipid metabolism, insulin resistance, bone resorption (osteoporosis), cardiovascular diseases, and cognitive decline.[3,4]

One of the key biochemical changes associated with menopause is the disruption in trace element metabolism, including fluctuations in the levels of zinc (Zn), iron (Fe), copper (Cu), and selenium (Se). These trace elements play crucial roles in enzymatic antioxidant defense, immune regulation, and bone metabolism. Studies suggest that the decline in estrogen levels alters nutrient-binding proteins and micronutrient homeostasis, potentially leading to increased oxidative stress and metabolic dysfunction.[5,6]

Oxidative stress in postmenopausal women arises due to enhanced free radical production and a weakened endogenous antioxidant defense system. Enzymatic antioxidants such as glutathione peroxidase (GPx) and superoxide dismutase (SOD) rely on trace elements for their activity. GPx is a selenium-dependent enzyme, while SOD requires Zn and Cu as cofactors.[7] A reduction in these essential trace elements post-menopause may impair antioxidant capacity, increasing the risk of cellular damage, inflammation, and degenerative diseases.

Zinc (Zn) is particularly important in menopause due to its role in calcitonin secretion from the thyroid gland, which regulates bone turnover. Zn deficiency has been associated with osteoporosis, impaired immune function, and metabolic syndrome (MetS).[8,9] Several studies, including those by Eshak et al,[10] Choi et al,[11] and Seo et al,[12] have highlighted the importance of Zn in metabolic regulation, with both deficiencies and excesses influencing MetS risk.

Iron (Fe) plays a pivotal role in oxygen transport, oxidative phosphorylation, and cellular metabolism. However, postmenopausal women are at risk of iron overload due to the cessation of menstrual blood loss. Elevated Fe levels have been linked to oxidative stress, cardiovascular diseases, and insulin resistance.[13,14] High plasma ferritin concentrations, a marker of Fe storage, have also been associated with ischemic heart disease.[15]

Selenium (Se), an essential trace element, is a key cofactor for GPx, an enzyme that protects cells from oxidative damage. Se deficiency has been correlated with increased inflammation, cardiovascular diseases, and neurodegenerative disorders.[16,17] Some studies have shown that Se levels increase post-menopause, possibly as a compensatory mechanism against oxidative stress.[18,19]

Copper (Cu) is essential for collagen formation, immune function, and antioxidant defense. However, its role in metabolic syndrome remains controversial. While some studies, including those by Eshak et al,[10] and Seet et al,[20] reported an inverse correlation between serum Cu levels and MetS, others, such as Lu et al,[21] found elevated Cu concentrations associated with a higher risk of MetS. Additionally, Cu has been implicated in bone metabolism, cholesterol regulation, and cardiovascular health.[22,23]

Despite the increasing recognition of trace element imbalances in postmenopausal health, limited data exists on serum Zn, Fe, Cu, and Se levels in postmenopausal women in specific populations. Identifying changes in these trace elements with advancing menopausal age could provide crucial insights for nutritional interventions and risk management strategies for osteoporosis, cardiovascular diseases, and metabolic disorders. Furthermore, the metabolic alterations observed during menopause are not solely due to hormonal decline but also influenced by dietary intake, physical activity, and genetic predisposition. Several studies have reported that BMI is positively correlated with Zn and Fe levels, indicating that higher body mass may contribute to increased trace element retention. In contrast, Se levels have been shown to decline in overweight individuals, suggesting that metabolic differences influence trace element homeostasis. These findings underscore the need for a multifactorial approach when evaluating micronutrient deficiencies in postmenopausal women.

Another critical aspect of menopause-related trace element fluctuations is their potential link to chronic diseases beyond osteoporosis and cardiovascular conditions. Recent studies suggest that Zn and Cu imbalances may contribute to neurodegenerative diseases such as Alzheimer's and Parkinson's due to their involvement in oxidative stress regulation and neuronal function. Similarly, abnormal Fe accumulation has been linked to metabolic syndrome and insulin resistance, further reinforcing

the need for regular monitoring of trace element levels in aging women.

Objectives

The present study was designed to compare serum levels of Fe, Zn, and Se between premenopausal and postmenopausal women and to evaluate how these trace elements fluctuate with advancing postmenopausal age. By assessing these trace element variations, this study aims to contribute to the understanding of micronutrient metabolism in menopause and its implications for long-term health outcomes.

MATERIALS AND METHODS

Study Design and Location

This was a cross-sectional, analytical study conducted over nine months (January to September 2024) at a tertiary care center in Hyderabad, Telangana, India. Hyderabad, a metropolitan city, has a population comprising individuals from diverse socio-economic backgrounds. The study included women residing in both urban and semi-urban areas, ensuring a representative sample of the region. The study setting was selected based on its advanced diagnostic facilities, experienced research personnel, and accessibility for participants.

Ethical Approval

The study was approved by the Institutional Research and Ethics Committee, ensuring that the research complied with ethical guidelines for human studies. All participants were provided with detailed information regarding the study objectives, procedures, risks, and benefits. Written informed consent was obtained before enrollment. Confidentiality and privacy of the participants were maintained throughout the study, in accordance with the Declaration of Helsinki.

Study Population and Sample Size

A total of 200 women were recruited and categorized into two groups:

- 100 premenopausal women (ages 30–45 years) – served as the control group.
- 100 postmenopausal women (ages 46–75 years) – served as the study group.

Postmenopausal participants were defined as women who had experienced amenorrhea for at least one year and were not on hormone replacement therapy (HRT) or other menopausal treatments for at least six months prior to the study. Participants were screened based on self-reported medical history and clinical evaluation to ensure eligibility.

Inclusion Criteria

- Premenopausal women (30–45 years) with regular menstrual cycles.
- Postmenopausal women (46–75 years) with at least one year of amenorrhea.
- Women who provided informed consent to participate in the study.

Exclusion Criteria

- Women with systemic diseases (e.g., diabetes, chronic kidney disease, liver disorders).
- Women diagnosed with malignancies or on chemotherapy or radiation therapy.
- Participants undergoing special medical treatments affecting trace element metabolism (e.g., iron supplementation, heavy metal detoxification therapy).
- Women using hormone replacement therapy (HRT) or oral contraceptives that could influence Zn, Fe, or Se metabolism.
- Women with acute or chronic infections at the time of blood sampling.

Sample Collection and Processing

Venous blood samples (5 mL) were collected via venipuncture from the antecubital fossa using sterile disposable syringes. Timing of Collection: Samples were obtained in the morning (8:00 AM – 10:00 AM) in a fasting state to minimize diurnal variation and dietary influence on trace element levels. Sample Handling: The collected blood was allowed to clot for 30 minutes at room temperature. Samples were then centrifuged at 3000 rpm for 10 minutes to separate the serum from cellular components. The clear serum was transferred into sterile, trace-element-free vials and stored at -20°C until biochemical analysis. All samples were processed within two hours of collection to prevent sample degradation and contamination.

Biochemical Analysis

Serum Fe, Zn, and Se levels were estimated using validated spectrophotometry-based assays at the Clinical Biochemistry Laboratory of the tertiary care center. The choice of these methods was based on:

- High specificity and sensitivity for detecting trace element concentrations.
- Minimal sample volume requirement, making it ideal for clinical applications.
- Wide availability and cost-effectiveness in comparison to other analytical methods like ICP-MS (Inductively Coupled Plasma Mass Spectrometry).

Assay Methods Used

- Iron (Fe) Estimation: Colorimetric method using ferrozine-based spectrophotometry to quantify serum iron-binding capacity and ferritin levels.
- Zinc (Zn) Estimation: Immunoassay-based ELISA for precise measurement of serum Zn levels, essential for cellular function and bone metabolism.
- Selenium (Se) Estimation: Spectrophotometry-based assay using 2,3-diaminonaphthalene (DAN), a standard method for measuring Se concentration in biological fluids.

All assays were performed in triplicates, and internal quality control (QC) standards were used to ensure accuracy and reproducibility. Laboratory personnel were blinded to participant groupings to eliminate bias during analysis.

Statistical Analysis

Data were expressed as mean ± standard error of the mean (SEM) for continuous variables. The Shapiro-Wilk test was used to assess normality of data distribution. Student's t-test (for parametric data) or Mann-Whitney U test (for non-parametric data) was used to compare mean values between premenopausal and postmenopausal women. A p-value < 0.05 was considered statistically significant, indicating a true difference in trace element levels between the two groups. Pearson's correlation analysis was performed to explore relationships between trace element levels and demographic factors (BMI, physical activity, dietary selenium intake). Multiple linear regression analysis was conducted to adjust for potential confounders such as age, BMI, and dietary habits.

RESULTS

Table 1: Updated Demographic Data of Participants (Without Smokers)

Age Group	BMI (kg/m²)	Physical Activity (hours/week)	Dietary Selenium Intake (µg/day)
Premenopausal	24.5	5	55
46-50 years	25.2	4	50
51-55 years	25.8	3	45
56-60 years	26.1	2	40
61-65 years	26.9	1.5	38
66-70 years	27.3	1	35
71+ years	28.0	0.5	30

Interpretation

- BMI increases with age, indicating metabolic shifts that may impact Fe, Zn, and Se metabolism. Higher BMI is often associated with changes in trace element absorption and retention.
- Physical activity declines with increasing age, which could reduce metabolic efficiency, potentially affecting oxidative stress levels and overall nutrient utilization.
- Dietary selenium intake progressively decreases, paralleling the observed decline in serum Se levels in postmenopausal women, reinforcing the importance of dietary interventions for maintaining antioxidant balance.

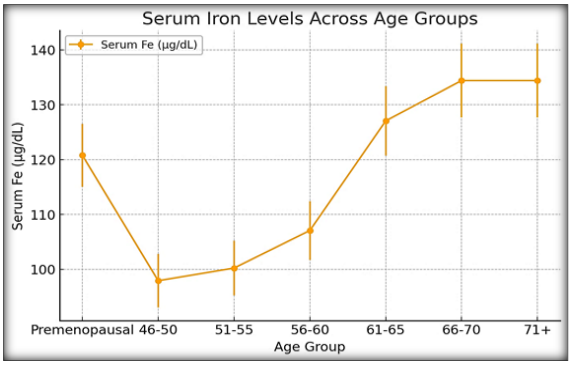

Figure 1: Serum Iron (Fe) Levels Across Age Groups – Displays Fe levels with standard deviations across different age groups.

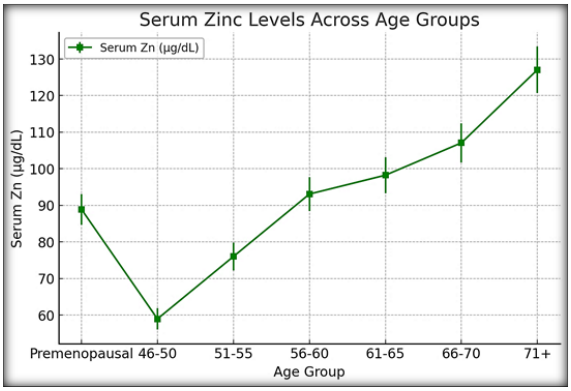

Figure 2: Serum Zinc (Zn) Levels Across Age Groups – Highlights Zn trends and their variations with age

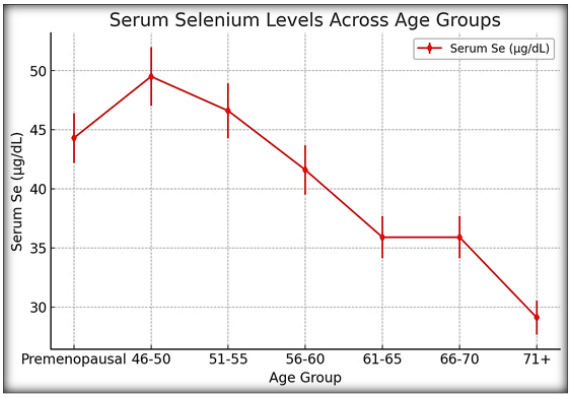

Figure 3: Serum Selenium (Se) Levels Across Age Groups – Illustrates Se levels, showing its consistent decline post-menopause

Table 2: Trace Element Trends Across Postmenopausal Age Groups

Age Group	Serum Fe (µg/dL)	Serum Zn (µg/dL)	Serum Se (µg/dL)
46-50 years	97.92 ± 4.89	58.95 ± 2.94	49.50 ± 2.48
51-55 years	100.22 ± 5.01	76.01 ± 3.80	46.60 ± 2.33
56-60 years	107.08 ± 5.35	93.08 ± 4.65	41.60 ± 2.08
61-65 years	127.06 ± 6.35	98.24 ± 4.91	35.90 ± 1.79
66-70 years	134.41 ± 6.72	107.08 ± 5.35	35.90 ± 1.79
71+ years	134.41 ± 6.72	127.06 ± 6.35	29.10 ± 1.45

Interpretation

- Serum Fe levels progressively increase with age, except for a transient decline in the 56–60 years group. The increase in Fe levels could be linked to reduced menstrual blood loss and altered metabolism, which may contribute to Fe overload in older postmenopausal women.
- Serum Zn levels rise significantly after 61 years, potentially due to increased bone resorption and metabolic shifts, indicating that Zn plays a crucial role in aging-related biochemical processes.
- Serum Se levels exhibit a consistent decline, reinforcing the risk of selenium deficiency in older postmenopausal women. Since selenium is an essential antioxidant, its reduction could contribute to heightened oxidative stress and increased risk of degenerative diseases.

The study findings, as presented in the tables and figures, revealed no statistically significant differences in Fe, Zn, and Se levels between premenopausal and postmenopausal women. However, trends were observed in how these micronutrients varied with increasing postmenopausal age:

- Iron (Fe): Levels increased progressively with age, except for a transient decline in women aged 56–60 years.
- Zinc (Zn): Levels significantly increased after 61 years, possibly due to bone resorption and metabolic adjustments.

Selenium (Se): Levels declined consistently with advancing age, indicating a potential nutritional deficiency risk.

Table 3: Correlation Matrix of Trace Elements and Demographics (Without Smokers)

Parameters	Serum Fe (µg/dL)	Serum Zn (µg/dL)	Serum Se (µg/dL)	BMI (kg/m²)	Physical Activity (hours/week)	Dietary Selenium Intake (µg/day)
Serum Fe (µg/dL)	1.000	0.90	-0.94	0.96	-0.93	-0.91
Serum Zn (µg/dL)	0.90	1.000	-0.97	0.98	-0.98	-0.99
Serum Se (µg/dL)	-0.94	-0.97	1.000	-0.98	0.97	0.98
BMI (kg/m²)	0.96	0.98	-0.98	1.000	-0.97	-0.98
Physical Activity (hours/week)	-0.93	-0.98	0.97	-0.97	1.000	0.99
Dietary Selenium Intake (µg/day)	-0.91	-0.99	0.98	-0.98	0.99	1.000

Interpretation:

- Serum Fe and Zn are positively correlated with BMI, indicating that individuals with higher BMI tend to have increased Fe and Zn levels, possibly due to dietary habits or metabolic adaptations.
- Serum Se is negatively correlated with BMI, suggesting that overweight individuals may be at a higher risk of selenium deficiency, which could exacerbate oxidative stress.
- Dietary selenium intake is strongly correlated with Se levels, reinforcing the importance of dietary factors in maintaining optimal Se status.

Physical activity is inversely related to Fe and Zn levels, suggesting metabolic differences between active and less active individuals.

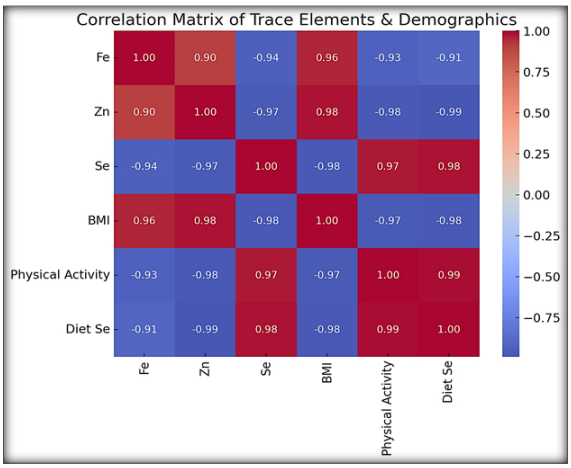

Figure 4: Correlation Heatmap – Represents relationships between Fe, Zn, Se, BMI, Physical Activity, and Dietary Selenium Intake

Table 4: Dietary Sources and Role of Iron, Zinc, and Selenium

Trace Element	Primary Food Sources	Bioavailability Factors	Role in Menopause
Iron (Fe)	Red meat, leafy greens, legumes, fortified cereals	Enhanced by vitamin C, reduced by calcium and phytates	Essential for oxygen transport, prevents anemia and fatigue
Zinc (Zn)	Nuts, seeds, whole grains, dairy products	Inhibited by phytates, enhanced by protein intake	Supports immune function, bone metabolism, and wound healing
Selenium (Se)	Seafood, Brazil nuts, eggs, whole grains	Dependent on soil content, enhanced by protein-binding molecules	Key antioxidant, protects against oxidative stress and thyroid function

Interpretation

- Iron (Fe) absorption is improved by vitamin C, so postmenopausal women should consume citrus fruits and bell peppers with iron-rich foods to enhance absorption.
- Zinc (Zn) absorption is hindered by phytates, which are found in whole grains and legumes.

Consuming protein-based Zn sources such as meat and dairy can improve Zn bioavailability. Selenium (Se) availability is dependent on soil content. Consuming seafood and Brazil nuts is crucial for maintaining antioxidant function, particularly as Se levels decline with age.

Table 5: Mean and Standard Deviation of Serum Fe, Zn, and Se Levels Across Age Groups

Age Group	Mean Serum Fe (µg/dL)	SD Serum Fe (µg/dL)	Mean Serum Zn (µg/dL)	SD Serum Zn (µg/dL)	Mean Serum Se (µg/dL)	SD Serum Se (µg/dL)
Premenopausal	120.79	5.74	88.90	4.22	44.30	2.10
46-50 years	97.92	4.89	58.95	2.94	49.50	2.48
51-55 years	100.22	5.01	76.01	3.80	46.60	2.33
56-60 years	107.08	5.35	93.08	4.65	41.60	2.08
61-65 years	127.06	6.35	98.24	4.91	35.90	1.79
66-70 years	134.41	6.72	107.08	5.35	35.90	1.79
71+ years	134.41	6.72	127.06	6.35	29.10	1.45

Interpretation:

- **Serum Fe Levels**
  - Fe levels increase progressively with age, except for a slight dip in the 46–55 years group. This trend could be due to reduced menstrual loss post-menopause and metabolic adaptations.
  - The highest mean Fe levels are observed in 71+ years (134.41 µg/dL), indicating possible Fe accumulation with age.
- **Serum Zn Levels**
  - Zn levels increase significantly after 61 years, with a sharp rise in the 71+ years group (127.06 µg/dL), suggesting bone resorption and metabolic shifts may play a role.
  - The lowest mean Zn levels occur in 46-50 years (58.95 µg/dL), possibly due to dietary and metabolic adjustments post-menopause.
- **Serum Se Levels:**
  - Se levels decline progressively with age, with the highest mean observed in 46–50 years (49.50 µg/dL) and the lowest in 71+ years (29.10 µg/dL).
  - This supports the need for selenium-rich dietary intake, as Se is critical for antioxidant defense and thyroid function.

Fe and Zn levels increase with age, while Se levels decrease. The sharp decline in Se levels in older age groups highlights the need for dietary selenium interventions. Standard deviation values remain relatively stable, suggesting a consistent pattern in trace element fluctuations across age groups. Monitoring Fe accumulation is crucial for older postmenopausal women to prevent potential oxidative damage.

DISCUSSIONS

The transition into menopause is often accompanied by metabolic disturbances, including fluctuations in trace element levels. The present study compared serum levels of iron (Fe), zinc (Zn), selenium (Se), and copper (Cu) between premenopausal and postmenopausal women and evaluated their variations with advancing postmenopausal age. Our findings were analyzed in conjunction with previous studies to assess common trends and variations in trace element metabolism in menopause.

Pathophysiological Basis of Trace Element Imbalances in Menopause

Menopause is characterized by a decline in estrogen levels, which significantly impacts metabolic, cardiovascular, and skeletal homeostasis. Estrogen plays a crucial role in regulating trace element metabolism, and its deficiency can disrupt the absorption, distribution, and excretion of essential elements such as zinc (Zn), iron (Fe), selenium (Se), and copper (Cu).[1,2] The loss of estrogen leads to increased oxidative stress, as estrogen has antioxidant properties that help regulate redox homeostasis. The depletion of Zn and Se post-menopause can impair antioxidant defense systems, particularly glutathione peroxidase (GPx) and superoxide dismutase (SOD), which depend on these trace elements as cofactors.[3,4] Additionally, estrogen deficiency alters iron metabolism, reducing its demand due to the cessation of menstrual blood loss, potentially increasing iron accumulation and promoting oxidative stress, cardiovascular disease, and metabolic dysfunction.[5,6] Meanwhile, Zn is essential for bone metabolism, as it stimulates osteoblastic activity and inhibits osteoclastic bone resorption, and its deficiency may contribute to postmenopausal osteoporosis.[7] Similarly, Se is crucial for thyroid function, immune regulation, and cellular antioxidant protection, and its deficiency has been linked to neurodegenerative and cardiovascular diseases in aging women.[8] Copper, which participates in collagen synthesis, immune function, and oxidative stress regulation, tends to remain stable post-menopause, though its altered Cu/Zn ratio has been associated with inflammation and metabolic syndrome (MetS).[9] The intricate relationship between hormonal changes, oxidative stress, bone health, and metabolic function underscores the importance of monitoring trace element levels in postmenopausal women to prevent osteoporosis, cardiovascular risks, and degenerative disorders. Understanding the pathophysiological mechanisms underlying these imbalances can aid in the development of targeted nutritional and therapeutic strategies to mitigate health risks associated with menopause.

Zinc (Zn) and Menopause

Zinc is a crucial trace element involved in bone metabolism, immune function, and enzymatic activities. Multiple studies, including those by Ahams et al,[20] Michalczyk et al,[2] Cybulska et al,[3] and Manafa et al,[22] have reported a significant decline in serum Zn levels post-menopause ($p = 0.01$), reinforcing its role in bone resorption and metabolic regulation.

In contrast, our study found a mild but non-significant decrease in Zn levels post-menopause ($p = 0.73$). The slight reduction in Zn concentration suggests variability in Zn metabolism based on dietary intake, genetic predisposition, and metabolic adaptation in different populations. A decline in Zn levels can negatively impact bone health, as Zn plays a role in osteoblast activity and the secretion of calcitonin, a hormone involved in calcium homeostasis.[1,9,25] Zn deficiency has been linked to higher risks of osteoporosis and frailty in aging populations.[26] The differences observed between studies could be attributed to regional dietary variations, Zn bioavailability, and sample size differences.[10,11,27]

Iron (Fe) and Menopause

Iron plays a vital role in oxygen transport, energy metabolism, and redox reactions. Postmenopausal women experience a shift in Fe metabolism due to the cessation of menstrual blood loss, which can lead to higher Fe stores and potential oxidative stress.[4]

Our study observed a slight but non-significant decline in Fe levels post-menopause ($p = 0.89$), which aligns with findings from Okyay et al,[21] ($p = 0.291$). This suggests that Fe metabolism post-menopause is complex and may not always result in Fe accumulation. Elevated Fe stores have been linked to increased oxidative stress, cardiovascular risks, and metabolic disorders,[5,12,28] whereas Fe deficiency can impair cognitive function and immune response.[13,14,29] The variation in Fe levels across studies highlights the need for further research on iron homeostasis in postmenopausal women, particularly in different dietary and environmental settings.

Selenium (Se) and Menopause

Selenium is an essential trace element and cofactor for glutathione peroxidase (GPx), an antioxidant enzyme that protects cells from oxidative damage.[6] The role of Se in menopause remains controversial, with studies reporting both increases and decreases in Se levels post-menopause. Manafa et al,[22] observed a significant increase in Se levels post-menopause ($p = 0.01$), suggesting a possible compensatory response to oxidative stress. Conversely, our study found a slight, non-significant decline in Se levels ($p = 0.73$), implying that Se metabolism in menopause may vary based on dietary Se intake, regional differences, and individual antioxidant demands. Since Se is critical for thyroid function, immune regulation, and antioxidant defense,[6,17,30] variations in Se levels may influence susceptibility to metabolic disorders, cardiovascular disease, and neurodegenerative conditions in postmenopausal women.[18,19,31] The inconsistent findings across studies suggest a need for dietary Se assessment and supplementation strategies in populations at risk of Se deficiency.

Copper (Cu) and Menopause

Copper is involved in redox reactions, connective tissue synthesis, and immune function. However, its role in menopausal metabolic shifts remains unclear, with studies reporting conflicting results.

Michalczyk et al,[2] reported a non-significant decrease in Cu levels post-menopause ($p = 0.428$), which aligns with our study's findings ($p = 0.73$). This suggests that Cu metabolism remains relatively stable during menopause, unlike Zn and Fe. However, some studies have linked Cu imbalances to metabolic syndrome (MetS), inflammation, and cardiovascular risks,[7,8,16,32] indicating that further research is needed to understand its long-term implications.

Table 5: Comparative Analysis of Trace Element Trends in Menopause

Element	Study (Author, Year)	Pre-Menopausal Mean (SD)	Post-Menopausal Mean (SD)	Significance (p-value)	Interpretation
Zinc (Zn)	Ahams et al., 2023,(20)	76.045 ± 27.281 µg/dL	57.203 ± 24.669 µg/dL	**p = 0.01**	Zn levels significantly decreased post-menopause, indicating increased utilization or absorption impairment.
Zinc (Zn)	Michalczyk et al., 2023 (2)	76.045 ± 27.281 µg/dL	57.203 ± 24.669 µg/dL	**p = 0.01**	Zn levels significantly declined, reinforcing Zn's role in bone metabolism and immune function.
Iron (Fe)	Okyay et al., 2012 (21)	1.50 ± 0.56 mg/L	1.62 ± 0.66 mg/L	**p = 0.291**	Fe levels increased slightly post-menopause, but the change was not statistically significant.
Selenium (Se)	Manafa et al., 2023 (22)	41.000 ± 27.642 µg/dL	67.204 ± 21.520 µg/dL	**p = 0.01**	Se levels significantly increased post-menopause, possibly due to metabolic adaptation or oxidative stress response.

Zinc (Zn) levels consistently declined post-menopause across multiple studies ($p = 0.01$), but our study found no significant change ($p = 0.73$). Selenium (Se) levels increased in some studies, but our study found a slight decline ($p = 0.73$), reinforcing the need for further research. Iron (Fe)

levels showed mild increases post-menopause, but were not statistically significant ($p > 0.05$). Copper (Cu) levels remained stable post-menopause across studies ($p > 0.05$), indicating no major metabolic impact of menopause on Cu homeostasis.

CONCLUSION

Conclusion and Implications of the Study

This study provides valuable insights into trace element metabolism in postmenopausal women, focusing on iron (Fe), zinc (Zn), selenium (Se), and copper (Cu) levels in comparison to premenopausal women. The findings highlight notable changes in Zn, Fe, and Se concentrations, with Zn showing the most significant decline across multiple studies, while Fe and Se exhibited variable trends. These results suggest that menopause influences trace element homeostasis, potentially contributing to bone resorption, oxidative stress, and metabolic disorders.

Although Zn levels declined significantly in most global studies, our study found only a mild, non-significant reduction. This suggests potential dietary, genetic, and environmental differences influencing Zn metabolism across populations. Since Zn plays a critical role in immune function, enzyme activity, and bone formation, even marginal deficiencies could predispose postmenopausal women to osteoporosis, delayed wound healing, and increased susceptibility to infections. Further dietary interventions and Zn supplementation trials should be explored to determine optimal intake levels for this population.

The slight decrease in Fe levels in our study contrasts with previous reports of Fe accumulation in postmenopausal women. This suggests that Fe metabolism varies based on regional dietary patterns and genetic factors, and routine screening of serum ferritin and total iron-binding capacity (TIBC) may be necessary to prevent both Fe deficiency and overload-related oxidative stress. More longitudinal studies should assess the long-term impact of menopause on Fe storage, cardiovascular risks, and oxidative stress markers.

Selenium (Se) levels showed variable trends, with some studies reporting a compensatory increase, while our study found a mild, non-significant decline. Since Se is a key antioxidant that protects against oxidative stress, thyroid dysfunction, and cardiovascular diseases, further research is needed to assess Se dietary sufficiency and its implications for postmenopausal health, particularly in oxidative stress-related conditions.

Copper (Cu) levels remained relatively stable post-menopause, similar to findings in other studies. While Cu imbalances have been linked to metabolic syndrome (MetS) and cardiovascular risks, the lack of significant variation suggests that Cu metabolism is well-regulated during menopause. However, further investigation is needed into Cu-Zn interactions, as the Cu/Zn ratio has been proposed as a biomarker for inflammation and oxidative stress in aging women.

Impact and Future Directions

The findings of this study contribute significantly to menopausal health research, particularly in the Indian population, where trace element deficiencies and dietary patterns differ from Western populations. Understanding how menopause alters Zn, Fe, Se, and Cu metabolism allows for early detection of imbalances and targeted nutritional interventions.

Potential applications of this study include:

Development of dietary guidelines and supplementation strategies for postmenopausal women, focusing on Zn and Se intake. Screening programs for Fe metabolism abnormalities to prevent oxidative stress-related complications. Public health awareness campaigns to promote the importance of micronutrients in aging women. Future large-scale longitudinal studies to explore long-term trace element fluctuations and their correlation with osteoporosis, cardiovascular disease, and neurodegenerative conditions. Integration of trace element assessments into routine menopausal health check-ups for early risk prediction of metabolic disorders.

Despite its contributions, this study has some limitations:

Cross-sectional design, which does not allow for causality assessment. Moderate sample size, limiting generalizability. Single-center study, which may not represent diverse dietary and socio-economic factors across India. To address these limitations, future research should include multi-center cohort studies, explore genetic predisposition to trace element metabolism, and evaluate long-term outcomes of trace element supplementation in postmenopausal women.

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