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Selenium, Copper and Zinc Levels in Female Subjects with Uterine Fibroid in Port Harcourt, Nigeria

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Abstract
Uterine fibroids are common benign tumors whose biological mechanisms remain incompletely understood. Altered trace-element homeostasis may be relevant to the oxidative and cellular processes associated with fibroid biology. This study examined serum selenium, copper, zinc, and copper/zinc ratio among women with uterine fibroids. The study included 140 women aged 20–50 years, comprising 80 participants with uterine fibroids and 60 controls. Serum selenium, copper, and zinc concentrations were determined using atomic absorption spectrophotometry, and the copper/zinc ratio was calculated. Between-group differences were evaluated using an independent-samples t-test, while differences according to disease duration were assessed using analysis of variance. Women with uterine fibroids had lower mean selenium and zinc concentrations than controls, whereas copper concentration and copper/zinc ratio were higher. The reported between-group differences were statistically significant. Among the 50 participants with available disease-duration data, no significant differences were observed in selenium, copper, zinc, or copper/zinc ratio across the three duration categories. The study provides population-specific evidence of altered serum trace-element profiles in women with uterine fibroids. The findings support further investigation of trace-element homeostasis as a potential component of fibroid biology, while longitudinal research is required to establish temporal relationships and clinical relevance.

INTRODUCTION

Uterine fibroids, also known as uterine leiomyomas, are benign tumors arising from the smooth muscle cells of the myometrium and represent one of the most common gynecological disorders affecting women of reproductive age. Although histologically benign, fibroids can produce substantial clinical morbidity through heavy menstrual bleeding, pelvic pain and pressure, anemia, infertility, pregnancy complications, and impaired quality of life. Recent evidence indicates that fibroids affect a substantial proportion of women, with prevalence increasing markedly with age and considerable variation according to genetic, hormonal, metabolic, and environmental factors (Yang et al., 2022; Awiwi et al., 2022; Behairy et al., 2024; Dolmans et al., 2024; Bulun et al., 2025). Their clinical burden is particularly important because symptoms may persist for prolonged periods and frequently require pharmacological, minimally invasive, or surgical interventions. Contemporary management guidelines consequently emphasize individualized assessment and treatment, while recognizing that the underlying biological mechanisms of fibroid development remain incompletely understood (Makary et al., 2024; Chen et al., 2025).

The current state of knowledge increasingly conceptualizes uterine fibroids as a multifactorial disease involving interactions among sex-steroid signaling, genetic alterations, extracellular-matrix accumulation, cellular proliferation, inflammation, immune dysregulation, and oxidative stress. Molecular studies have identified recurrent somatic alterations, particularly mutations involving the MED12 gene, while other pathways associated with growth-factor signaling, extracellular-matrix remodeling, and cellular metabolism also contribute to leiomyoma development and progression (Amendola et al., 2024; Yang et al., 2022; Dolmans et al., 2024). In parallel, emerging evidence indicates that inflammatory and immune processes are closely involved in fibroid biology, including the local inflammatory environment and tissue remodeling that accompany tumor growth (Ishikawa et al., 2024; Don et al., 2022). Oxidative stress has likewise received increasing attention because excessive reactive oxygen species may disrupt cellular redox homeostasis, promote DNA and protein damage, alter signaling pathways, and facilitate abnormal smooth-muscle-cell survival and extracellular-matrix deposition (AlAshqar et al., 2023; Maghraby et al., 2022; Lin et al., 2023). These developments suggest that biochemical factors capable of regulating antioxidant defense and cellular redox balance may be relevant to the pathophysiology of uterine fibroids.

Among these biochemical factors, selenium, zinc, and copper are biologically important trace elements with interconnected roles in antioxidant defense, enzymatic activity, cellular proliferation, immune regulation, and reproductive physiology. Selenium is incorporated into selenoproteins involved in redox regulation and antioxidant protection, whereas zinc contributes to numerous enzymatic, structural, transcriptional, and cellular functions. Copper is essential for several metabolic enzymes and participates in redox-related processes, although excessive or dysregulated copper availability may contribute to oxidative imbalance (Jomova et al., 2025; Huang et al., 2026; Afzal et al., 2023; An et al., 2022; Saporito Magriñá et al., 2026). Importantly, the biological relevance of these elements cannot always be interpreted independently because their concentrations may interact functionally, making the copper/zinc ratio a potentially informative indicator of altered trace-element homeostasis (Lima et al., 2022; Costa et al., 2023; Peng et al., 2024). Research in reproductive medicine has also demonstrated that circulating or follicular concentrations of selenium, zinc, and copper may be associated with female reproductive function and reproductive outcomes, reinforcing the importance of investigating trace-element status within gynecological populations (Klein et al., 2023; Li et al., 2022; Zhao et al., 2022).

Recent empirical evidence provides a stronger rationale for examining trace elements in women with gynecological disorders. A case-control investigation involving women with endometrial diseases reported significantly lower serum selenium and zinc concentrations but higher copper concentrations, together with an elevated copper/zinc ratio, compared with healthy women (Zhang et al., 2022; Pokorska-Niewiada et al., 2025; Chaudhary et al., 2025). These findings are particularly relevant to uterine fibroids because they suggest that altered trace-element homeostasis may accompany pathological conditions affecting the female reproductive system. Other research has demonstrated associations between copper, zinc, and selenium status and reproductive outcomes, although the direction and magnitude of these relationships vary according to population, physiological condition, biological matrix, and potential confounding factors (Klein et al., 2023; Li et al., 2022; Wang et al., 2022). Evidence from broader female populations further indicates that serum concentrations of these micronutrients are influenced by sociodemographic and nutritional characteristics, emphasizing the need for population-specific investigation rather than assuming uniform trace-element profiles across populations (Peng et al., 2024; Costa et al., 2023; Mohy, 2026).

Despite these advances, an important knowledge gap remains. The contemporary literature on uterine fibroids has concentrated predominantly on genetic mechanisms, hormonal regulation, extracellular-matrix remodeling, inflammation, oxidative stress, imaging, and clinical management, whereas comparatively less attention has been directed toward the comparative biochemical profile of essential trace elements in women with established fibroids. Although previous research has reported associations between trace-element status and endometrial or reproductive disorders, evidence specifically characterizing selenium, copper, zinc, and the copper/zinc ratio among women with uterine fibroids remains limited. Moreover, findings from studies conducted in different geographical and nutritional contexts cannot automatically be generalized to women in sub-Saharan Africa. This limitation is important because trace-element status is influenced by dietary intake, environmental exposure, socioeconomic conditions, and demographic characteristics, all of which may vary substantially between populations (Costa et al., 2023; Peng et al., 2024). Consequently, locally generated biochemical evidence is necessary to determine whether patterns reported elsewhere are also observable among women with uterine fibroids in Nigeria.

The present study addresses this gap by examining serum selenium, copper, zinc, and copper/zinc ratio among women with uterine fibroids in Port Harcourt, Nigeria, using a comparative cross-sectional design with women without fibroids as controls. The study specifically investigates whether these biochemical parameters differ between the fibroid and control groups and whether trace-element profiles vary according to the duration of the fibroid condition. The novelty of the study lies in providing population-specific comparative evidence on the combined profile of selenium, copper, zinc, and copper/zinc ratio in women with uterine fibroids in the Nigerian context. By integrating these four biochemical indicators within a single comparative framework, the study contributes additional empirical evidence to the growing literature on the relationship between trace-element homeostasis and gynecological disease. The findings are expected to strengthen the biochemical understanding of uterine fibroids, provide a basis for future longitudinal and mechanistic research, and help determine whether altered trace-element profiles warrant further investigation as potential biomarkers of uterine fibroid-related biological changes.

METHODS

Study Design and Setting

This study employed a cross-sectional comparative design to determine and compare serum selenium, copper, zinc, and copper/zinc ratio among women with uterine fibroids and women without fibroids in Port Harcourt, Nigeria. The design was selected because the study aimed to characterize biochemical differences between the two groups at a defined period without introducing an experimental intervention. The methodological reporting was structured in accordance with the principles recommended for observational cross-sectional studies, particularly with respect to participant eligibility, selection, measurement procedures, study size, and statistical analysis. The study was conducted in Port Harcourt, Rivers State, Nigeria, through the relevant clinical and laboratory facilities.

Study Population, Sample Size, and Participant Selection

The study population comprised women aged 20–50 years. A total of 140 participants were included, consisting of 80 women diagnosed with uterine fibroids and 60 women without fibroids who served as the control group. The original study determined the sample size using G*Power version 3.1.9.2, assuming a statistical power of 95%, significance level of 0.05, and effect size of 0.80. G*Power is an established software package for prospective statistical power analysis and sample-size determination (Faul et al., 2009). The final allocation of participants therefore comprised 57.1% women with uterine fibroids and 42.9% controls. Participants were selected according to predefined eligibility criteria. The fibroid group included women aged 20–50 years with uterine fibroids who did not smoke, whereas controls were women within the same age range without uterine fibroids. Women who smoked or had serious medical conditions, including heart disease, kidney disease, diabetes mellitus, or other major health conditions, were excluded.

Data Collection and Study Instruments

Demographic information was obtained using a structured questionnaire administered to eligible participants. The questionnaire was used to collect relevant demographic characteristics, although the original manuscript does not provide sufficient information regarding its development, validation, or reliability. For the revised manuscript, the authors should specify whether the questionnaire was adapted from a previously validated instrument or developed specifically for this study and should report any pilot testing or reliability assessment if performed. No reliability coefficient should be reported unless it was actually calculated from the study data. Written informed consent was obtained from participants before enrollment. Ethical approval information, including the name of the approving committee and approval number, should be added to the final manuscript because the study involved human participants and venous blood collection.

Blood Collection and Laboratory Analysis

Venous blood samples were collected from each participant and transferred into plain sample bottles. The original methodology reports collection of 10 mL of whole blood, followed by centrifugation at 3,500 rpm for 5 minutes. The resulting serum was transferred into plain bottles and stored at −4°C until analysis. Serum selenium, copper, and zinc concentrations were determined using atomic absorption spectrophotometry (AAS). Digested samples and reagent blanks were analyzed, and the instrument was calibrated using standard solutions for copper, zinc, and selenium before measurement. Because trace-element measurements are sensitive to analytical variation and potential contamination, the revised manuscript should additionally report the AAS manufacturer and model, analytical wavelengths for each element, digestion reagents and procedure, calibration range, quality-control procedures, and analytical detection limits where available. Such information is important for analytical reproducibility and interpretation of trace-element measurements.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 27. Continuous variables were summarized as mean and standard deviation (SD). Differences in selenium, copper, zinc, and copper/zinc ratio between the fibroid and control groups were assessed using an independent-samples *t*-test, while one-way analysis of variance (ANOVA) was used to compare biochemical parameters across categories of fibroid duration. Statistical significance was established at $p \leq 0.05$. For improved statistical transparency, the revised analysis should verify normality and variance assumptions before applying parametric tests and report mean differences with 95% confidence intervals alongside *p*-values. The number of observations included in each analysis and any missing observations should also be explicitly reported, consistent with STROBE recommendations.

RESULTS AND DISCUSSION

Study Participants and Analytical Sample

A total of 140 female participants aged 20–50 years were included in the study. The study population consisted of 80 women with uterine fibroids and 60 women without uterine fibroids who served as the control group. Thus, women with uterine fibroids accounted for 57.1% of the total study population, while the control group accounted for 42.9%. The participant selection followed the eligibility criteria described in the methodology, including the restriction to non-smoking women and the exclusion of participants with major medical conditions such as heart disease, kidney disease, diabetes mellitus, or other serious health conditions.

The primary biochemical analysis was performed using the complete study groups of 80 fibroid participants and 60 controls. Serum selenium, copper, and zinc concentrations were determined for comparison between the two groups, and the copper/zinc ratio was subsequently evaluated as an additional biochemical indicator. The results were summarized using mean and standard deviation and compared using the independent-samples *t*-test. Demographic information was collected using a structured questionnaire. However, the available manuscript does not report the numerical distribution of the individual demographic characteristics obtained from the questionnaire. Consequently, variables such as mean age, age-category distribution, marital status, parity, occupation, educational level, or other demographic characteristics cannot be quantitatively presented from the available study document. This should be addressed in the final manuscript if the original questionnaire dataset or SPSS output is available.

Table 1. Composition of the Study Population

Study group	Number of participants	Percentage
Women with uterine fibroids	80	57.1%
Women without uterine fibroids (control)	60	42.9%
Total	140	100.0%

Source: Primary study participant records, processed by the authors

The primary comparison therefore provides a clear two-group analytical framework consisting of 80 participants with uterine fibroids and 60 controls. A separate analysis was subsequently conducted to determine whether serum trace-element concentrations varied according to the reported duration of uterine fibroids.

Comparative Serum Selenium Concentrations

The comparison of serum selenium concentrations demonstrated a lower mean value among women with uterine fibroids than among women in the control group. As shown in Table 3.2, the mean selenium concentration in the fibroid group was 7.92 ± 0.38 µg/dl, whereas the corresponding mean in the control group was 10.50 ± 0.66 µg/dl. Thus, the observed mean concentration was numerically lower among women with uterine fibroids.

Table 2. Comparison of Selenium, Copper, Zinc, and Copper/Zinc Ratio between Study Groups

Parameter	Fibroid subjects (n = 80) Mean ± SD	Control subjects (n = 60) Mean ± SD	*p*-value	*t*-value
Selenium (µg/dl)	7.92 ± 0.38	10.50 ± 0.66	0.010	42.740

Copper (µmol/dl)	1.38 ± 0.08	1.08 ± 0.05	<0.001	22.052
Zinc (µmol/dl)	0.74 ± 0.05	1.19 ± 0.06	0.031	23.962
Copper/Zinc ratio	1.89 ± 0.16	0.91 ± 0.06	<0.001	39.894

Source: Primary laboratory measurements obtained from study participants and processed by the authors

The reported statistical comparison produced a *p*-value of 0.010, indicating a statistically significant difference according to the significance criterion specified in the methodology ($p \leq 0.05$). The reported *t*-value was 42.740. The direction of the difference was consistent with the overall biochemical pattern observed in the study, with the fibroid group exhibiting a lower measured selenium concentration than the control group.

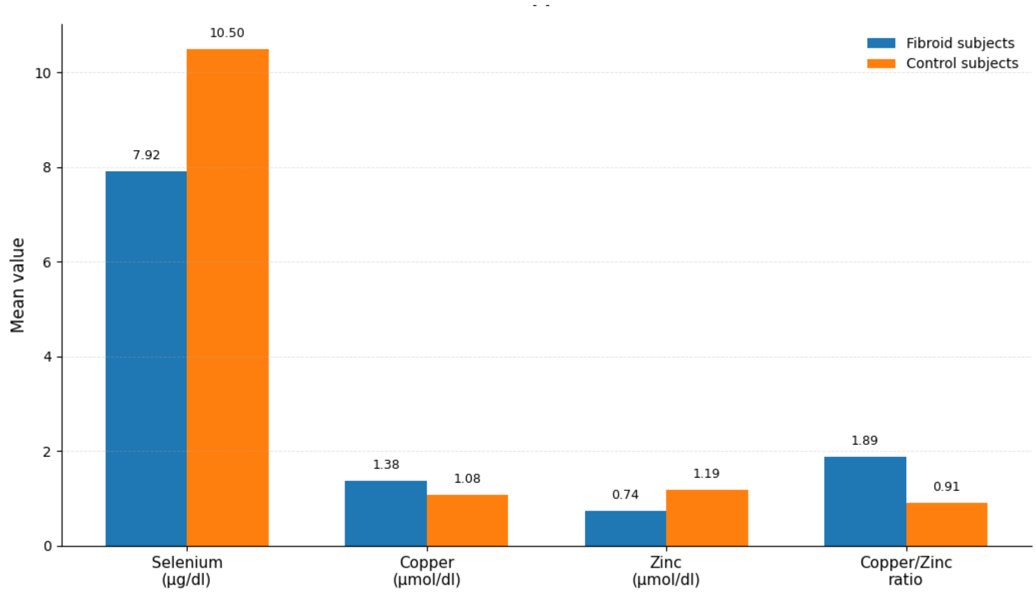

Figure 1. Comparative Mean Levels of Selenium, Copper, Zinc, and Copper/Zinc Ratio

Source: Primary laboratory data from 140 study participants, processed by the authors, 2026

Figure 1 Comparative mean levels of selenium, copper, zinc, and copper/zinc ratio between women with uterine fibroids and control subjects. The figure presents the mean values of the four biochemical parameters in the fibroid and control groups. Selenium and zinc showed lower mean values among women with uterine fibroids, whereas copper and the copper/zinc ratio showed higher mean values. Source: Primary laboratory data from study participants, processed by the authors.

Comparative Serum Copper Concentrations

The second component of the analysis assessed whether the biochemical parameters differed according to the duration of uterine fibroids. Participants with available disease-duration information were divided into three categories: 1–5 years, 6–10 years, and 10 years or more. The respective sample sizes were 30, 11, and 9 participants. Consequently, the reported duration analysis included 50 women with uterine fibroids rather than the complete group of 80.

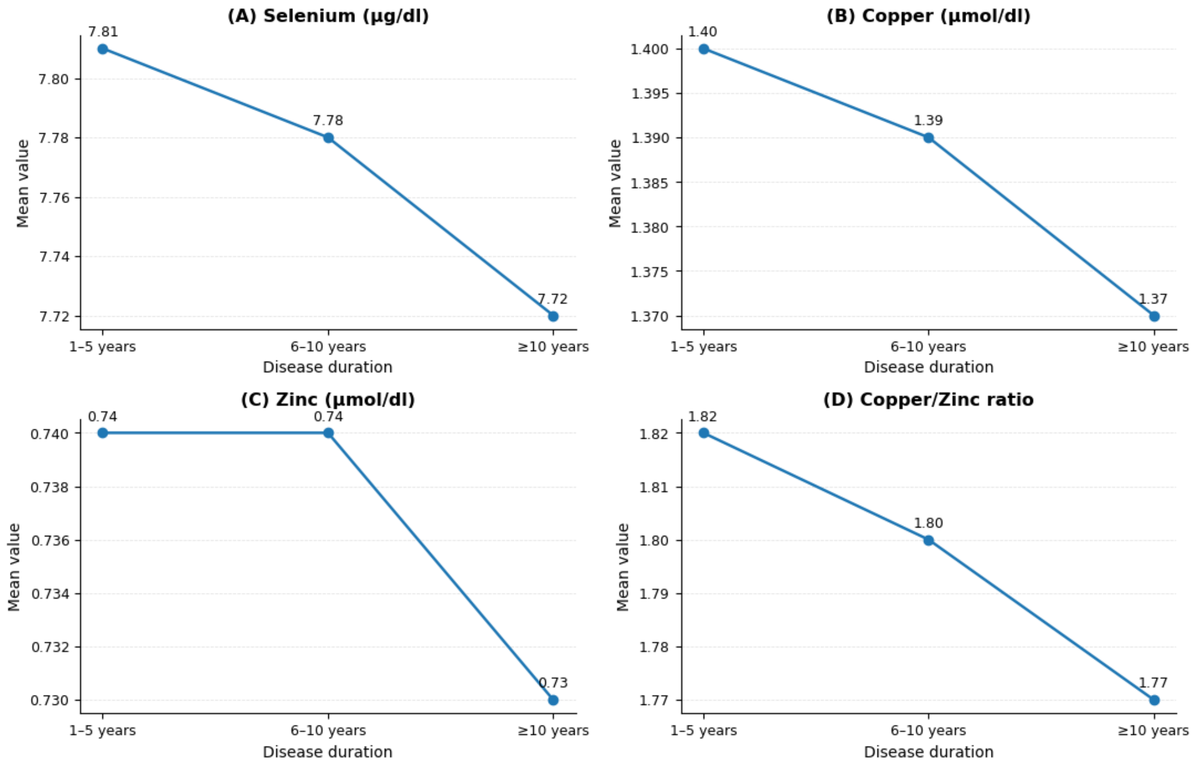

Figure 2. Trace-element profiles according to disease duration. (A) Selenium, (B) copper, (C) zinc, and (D) copper/zinc ratio among women with uterine fibroids according to disease-duration categories. Values represent mean concentrations or ratios.

Figure 2 illustrates the trace-element profiles across the three disease-duration categories. Selenium showed a gradual numerical decrease from 7.81 ± 0.73 in the 1–5-year group to 7.72 ± 0.57 in the ≥10-year group. Copper similarly decreased from 1.40 ± 0.08 to 1.37 ± 0.08 µmol/dl, while zinc remained relatively stable between the first two categories before decreasing slightly in the ≥10-year group. The copper/zinc ratio also showed a gradual numerical decline across the duration categories.

The analysis of serum zinc demonstrated a pattern similar to selenium but opposite to copper. Women with uterine fibroids had a mean zinc concentration of 0.74 ± 0.05 µmol/dl, whereas the control group had a mean concentration of 1.19 ± 0.06 µmol/dl. The reported *p*-value was 0.031 and the corresponding *t*-value was 23.962. According to the reported statistical criterion, the difference was statistically significant. The lower zinc concentration in the fibroid group, together with the higher copper concentration observed in the same participants, resulted in a marked difference in the copper/zinc ratio between the two groups.

The findings for selenium and zinc consequently showed a consistent direction, with both elements having lower mean concentrations among women with uterine fibroids than among controls. This contrasts with the copper finding, which showed a higher mean concentration in the fibroid group. The copper/zinc ratio showed the largest directional distinction among the biochemical indicators assessed in the study. The mean copper/zinc ratio was 1.89 ± 0.16 among women with uterine fibroids compared with 0.91 ± 0.06 among controls. The reported *p*-value was less than 0.001, while the *t*-value was 39.894.

The higher ratio among women with uterine fibroids was consistent with the simultaneous increase in copper and decrease in zinc observed in the primary comparison. Therefore, the ratio analysis reinforced the individual trace-element findings rather than demonstrating a contradictory pattern. The four biochemical measures demonstrated a coherent group-level pattern. Selenium and zinc concentrations were lower among women with uterine fibroids, whereas copper concentration and the copper/zinc ratio were higher. The statistical results reported in the original study indicated significant differences for all four parameters under the stated $p \leq 0.05$ criterion.

Comparison of Biochemical Parameters According to Disease Duration

The second component of the analysis assessed whether the biochemical parameters differed according to the duration of uterine fibroids. Participants with available disease-duration information were divided into three categories: 1–5 years, 6–10 years, and 10 years or more. The respective sample sizes were 30, 11, and 9 participants. Consequently, the reported duration analysis included 50 women with uterine fibroids rather than the complete group of 80.

Table 3. Serum Selenium, Copper, Zinc, and Copper/Zinc Ratio According to Duration of Uterine Fibroids

Disease duration	n	Selenium	Copper	Zinc	Copper/Zinc ratio
1–5 years	30	7.81 ± 0.73	1.40 ± 0.08	0.74 ± 0.06	1.82 ± 0.22
6–10 years	11	7.78 ± 0.64	1.39 ± 0.09	0.74 ± 0.06	1.80 ± 0.35
≥10 years	9	7.72 ± 0.57	1.37 ± 0.08	0.73 ± 0.05	1.77 ± 0.24
p-value	—	0.171	0.570	0.886	0.322
F-value	—	1.693	0.569	0.121	0.985

Source: Primary laboratory measurements among women with uterine fibroids, processed by the authors

The selenium concentration showed a gradual numerical decline across the three duration categories. The mean concentration was 7.81 ± 0.73 among women with a disease duration of 1–5 years, 7.78 ± 0.64 among those with 6–10 years, and 7.72 ± 0.57 among those with a duration of 10 years or more. Despite this numerical pattern, the reported *F*-value of 1.693 and *p*-value of 0.171 indicate that the difference did not reach statistical significance at the 0.05 level. Copper concentrations showed a similarly modest numerical pattern. The highest mean copper concentration was observed in the 1–5-year group at 1.40 ± 0.08 μmol/dl. This was followed by 1.39 ± 0.09 μmol/dl in the 6–10-year group and 1.37 ± 0.08 μmol/dl among participants with a disease duration of 10 years or more. The reported *F*-value was 0.569 and the *p*-value was 0.570, indicating no statistically significant difference among the duration groups.

The zinc concentrations were almost identical between the first two duration categories. The mean zinc concentration was 0.74 ± 0.06 μmol/dl in both the 1–5-year and 6–10-year groups, while the mean concentration was 0.73 ± 0.05 μmol/dl in the ≥10-year group. The reported *F*-value of 0.121 and *p*-value of 0.886 indicate no statistically significant variation in zinc concentration according to disease duration. The copper/zinc ratio also displayed only limited numerical variation across the disease-duration categories. The mean ratio was 1.82 ± 0.22 in the 1–5-year group, 1.80 ± 0.35 in the 6–10-year group, and 1.77 ± 0.24 in the ≥10-year group. The reported *F*-value was 0.985 and the *p*-value was 0.322. Accordingly, no statistically significant difference in the copper/zinc ratio was identified among the three duration categories.

The primary comparison included all 80 women with uterine fibroids and 60 control participants, whereas the disease-duration analysis was conducted among 50 women with uterine fibroids for whom duration data were available. The primary analysis demonstrated statistically significant differences in serum selenium, copper, zinc, and copper/zinc ratio between the fibroid and control groups. In contrast, none of these parameters differed significantly across the three disease-duration categories of 1–5 years, 6–10 years, and ≥10 years. The duration analysis should therefore be interpreted specifically for the 50 participants included in that analysis rather than generalized to the entire fibroid group. The available study record does not specify why 30 participants from the original fibroid group were not included in the duration analysis; this information should be clarified in the final manuscript if the underlying records are available.

Discussion

This study investigated the serum levels of selenium, copper, and zinc among women with uterine fibroids and compared these parameters with those of women without fibroids. The copper/zinc ratio was also examined as an integrated indicator of the relative balance between two biologically interacting trace elements. The principal finding was that women with uterine fibroids had lower serum selenium and zinc concentrations but higher copper concentrations and copper/zinc ratios than the control group. In contrast, none of the four biochemical parameters differed significantly according to the reported duration of uterine fibroids. These findings suggest that altered trace-element profiles may be associated with the presence of uterine fibroids, although the cross-sectional design does not permit conclusions regarding causality or temporal direction.

The lower selenium concentration observed among women with uterine fibroids is consistent with previous evidence linking selenium status with gynecological disease and oxidative balance (Li et al., 2023; Lima et al., 2022). The present study found a mean selenium concentration of 7.92 ± 0.38 μg/dl in the fibroid group compared with 10.50 ± 0.66 μg/dl among controls. Similar evidence has been reported by Okesola et al. (2022), who identified alterations in micronutrient and antioxidant-related parameters among women with uterine fibroids. More broadly, a case-control study involving women with endometrial diseases reported significantly lower serum selenium and zinc concentrations together with higher copper concentrations among affected women, providing an independent epidemiological context that is directionally consistent with the present findings. The biological plausibility of this association is supported by the role of selenium in selenoproteins involved in antioxidant defense, particularly glutathione peroxidase and thioredoxin-related pathways (Bayır et al., 2023; Gansemer & Rutkowski, 2022). Recent reviews of uterine fibroid biology have emphasized oxidative stress as one of the mechanisms potentially involved in leiomyoma development and progression. However, the present findings should not be interpreted as demonstrating that selenium deficiency causes uterine fibroids. Because selenium was measured after the condition was already established, reduced selenium may reflect altered nutritional status, disease-associated biological processes, or other unmeasured factors rather than being an initiating factor (Zheng et al., 2025).

The observed reduction in zinc provides an additional component of the altered trace-element profile. Zinc participates in numerous enzymatic and transcriptional processes and contributes to cellular antioxidant protection, immune regulation, DNA integrity, and tissue homeostasis (Molenda & Kolmas, 2023; Jomova et al., 2025; Chasapis et al., 2012). The present study found a mean serum zinc concentration of 0.74 ± 0.05 μmol/dl in women with uterine fibroids compared with 1.19 ± 0.06 μmol/dl in controls. This finding is consistent with evidence from previous studies reporting lower zinc concentrations among women with uterine or endometrial disorders. A case-control study of 302 women with endometrial diseases similarly found significantly lower serum zinc in affected participants, together with higher copper and lower selenium levels (Su et al., 2024; Simancas-Racines et al., 2025). Earlier evidence concerning uterine myoma has also reported reduced serum zinc in affected women compared with healthy controls, although the magnitude and direction of trace-element alterations have not been entirely uniform across populations. Such variation is important because circulating trace-element concentrations may be influenced by dietary intake, nutritional status, age, hormonal status, environmental exposure, and other population-specific characteristics. Accordingly, the present findings contribute population-specific evidence from Port Harcourt rather than establishing a universal biochemical profile for all women with uterine fibroids.

In contrast to selenium and zinc, serum copper was significantly higher among women with uterine fibroids (Li et al., 2023; Adhab et al., 2024). The mean copper concentration was 1.38 ± 0.08 μmol/dl in the fibroid group compared with 1.08 ± 0.05 μmol/dl in controls. This finding is directionally consistent with previous research showing higher serum copper among women with endometrial diseases and with earlier observations of altered copper concentrations in women with uterine myoma. Copper is an essential micronutrient involved in enzymatic reactions, cellular metabolism, and antioxidant-related processes; however, its biological effects are dependent on concentration and cellular context (Ukamaka et al., 2026; Tlak Gajger et al., 2025). Consequently, an elevated circulating copper concentration should not automatically be interpreted as evidence of pathological copper toxicity. It may instead reflect altered micronutrient homeostasis or physiological responses associated with the disease state. The concurrent reduction in zinc observed in this study is particularly relevant because copper and zinc are metabolically interconnected. Therefore, interpreting copper together with zinc may provide more information than considering either element independently (Michalczyk et al., 2023).

The elevated copper/zinc ratio represents an important finding of the present study. The mean ratio was 1.89 ± 0.16 among women with uterine fibroids compared with 0.91 ± 0.06 among controls. The ratio therefore differed in the same direction as the individual copper and zinc findings, namely higher copper combined with lower zinc. Previous research has proposed the Cu/Zn ratio as an indicator of altered trace-element balance and has examined its relationship with inflammatory, nutritional, immune, and oxidative processes. A recent study of infertile women in Port Harcourt also reported significant alterations in the copper/zinc ratio and examined its relationship with reproductive hormones, demonstrating the potential relevance of this ratio within reproductive health research. Evidence from women with endometrial diseases has likewise shown that higher Cu/Zn ratio values were associated with increased odds of disease in a dose-related analysis. Nevertheless, the elevated ratio observed in the present study should be interpreted as an association with altered trace-element balance, rather than as a direct biomarker of inflammation or oxidative stress (Islam et al., 2025; López-Alonso et al., 2025). The original manuscript interpreted the increased ratio as reflecting inflammation and oxidative stress, but no inflammatory cytokines, oxidative-stress biomarkers, or antioxidant enzyme activities were directly measured in this study. Therefore, such mechanisms remain biologically plausible explanations that require confirmation in future studies rather than conclusions established by the current data.

The findings can also be considered within the broader pathophysiology of uterine fibroids. Current evidence indicates that oxidative stress is involved in the complex biological environment of leiomyoma, together with extracellular-matrix remodeling, inflammatory signaling, hormonal regulation, and genetic alterations (Wang et al., 2026; Tatavarthi et al., 2026; Liu et al., 2025). Recent molecular research has further identified oxidative-stress-related biomarkers and pathways associated with uterine leiomyoma, supporting continued investigation of redox-related biological processes in fibroid development. From this perspective, the altered selenium, copper, and zinc concentrations observed in the present study may represent components of a broader disturbance in biochemical homeostasis. However, because the study did not measure reactive oxygen species, glutathione peroxidase, superoxide dismutase, catalase, C-reactive protein, interleukins, or other direct markers of oxidative or inflammatory activity, the relationship between the observed trace-element alterations and these mechanisms remains inferential.

An additional finding was the absence of statistically significant differences in selenium, copper, zinc, and copper/zinc ratio according to disease duration. Selenium decreased numerically from 7.81 in the 1–5-year group to 7.72 in the ≥10-year group, while copper decreased from 1.40 to 1.37 µmol/dl. Zinc remained relatively stable, ranging from 0.73 to 0.74 µmol/dl, and the copper/zinc ratio ranged from 1.82 to 1.77 across the three duration categories. None of these differences reached statistical significance. This result differs conceptually from the primary case-control comparison because disease duration analysis asks whether trace-element concentrations vary progressively after the fibroid condition has been established. The absence of a significant association therefore does not necessarily indicate that trace-element status is unrelated to fibroid biology. Rather, it suggests that the available data do not demonstrate a statistically significant difference across the reported duration categories.

Caution should be used in interpreting the duration finding as well, since only 50 of the 80 women with uterine fibroids were analyzed in the duration analysis. Thirty people had 1–5 years of disease duration, 11 people had 6–10 years of disease duration, and 9 people had ≥10 years. The smaller sample sizes in latter categories might lack statistical power to detect small differences. Moreover, disease duration does not necessarily equal the biological severity of the disease, extent of tumour load, or number of fibroids, fibroid site, or the accumulated exposure to disease-related physiological changes. One woman with a diagnosis of fibroids for a few years might have large fibroids, while another woman with a longer history might have clinically stable fibroids (Ahmad et al., 2023). Thus, the duration may not fully reflect the biological diversity of uterine fibroids. Studies need to take into account the duration along with fibroid size and number, location, symptom severity, treatment history, and related hormonal or inflammatory markers.

There are some caveats to take into account when interpreting these results. The cross-sectional design does not allow for determining whether the change in concentrations of the trace elements is a pre-existing condition prior to the development of fibroids or is a result of the disease. Secondly, the study was carried out in a particular population of women residing in Port Harcourt, Nigeria and results may not be directly applicable to women living in other geographical or nutritional settings. Thirdly, the data from the studies available are not comprehensive enough to include dietary intake, micronutrient supplementation, BMI, socioeconomic factors, menstrual characteristics or other potential confounding factors that could affect the concentrations of these nutrients in the blood. Fourth, only 50 of 80 women with uterine fibroids had disease-duration information, and the rationale for the missing disease-duration information needs to be explained. Lastly, the study did not directly evaluate tissue concentrations or oxidative and inflammatory biomarkers, but rather measured concentrations of the trace elements in the blood. The restrictions highlight the fact that the biochemical differences observed should be considered as associations that need to be further explored, but not as evidence for a defined mechanism.

In spite of these limitations, the study provides a contribution to the growing body of evidence on trace-elements homeostasis in uterine fibroids as it measured of selenium, copper, zinc and the copper to zinc ratio in women from Port Harcourt, Nigeria. The uniform direction of primary findings, which resulted in decreased levels of selenium and zinc and increased ratios of copper and Cu/Zn can be used to compare the pattern with the other populations. Past studies have shown that trace-element signatures can vary by reproductive and endometrial disease, and recent studies have highlighted the importance of oxidative and inflammatory mechanisms in the pathophysiology of uterine fibroids. The present findings thus are consistent with additional population-based and mechanistic studies, including longitudinal ones that could be used to determine whether the altered trace-element profile precedes fibroid development, evolves as the fibroids increase in number, or as a result of clinical treatment of the fibroids.

CONCLUSION

This study demonstrates a distinct serum trace-element profile among women with uterine fibroids compared with women without fibroids. Women with uterine fibroids exhibited lower selenium and zinc concentrations, whereas copper concentration and the copper/zinc ratio were higher. These findings indicate an association between uterine fibroid status and altered trace-element homeostasis, particularly involving the balance between copper and zinc. However, the absence of significant differences in selenium, copper, zinc, and copper/zinc ratio across disease-duration categories suggests that these biochemical alterations cannot be interpreted simply as progressive changes associated with longer disease duration.

The findings contribute population-specific evidence to the growing literature linking micronutrient homeostasis with the biological environment of uterine fibroids. Practically, the results provide a basis for further investigation of trace-element profiles as potential biochemical indicators, although their diagnostic or clinical utility cannot yet be established from the present evidence. The study is limited by its cross-sectional design, incomplete duration information, relatively small duration subgroups, and the absence of direct oxidative-stress, inflammatory, dietary, and nutritional assessments. Future longitudinal and mechanistic studies with larger and more comprehensively characterized populations are needed to determine temporal relationships and clinical relevance.

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