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Metabolomics unleashed: transforming disease diagnosis and treatment with molecular insights

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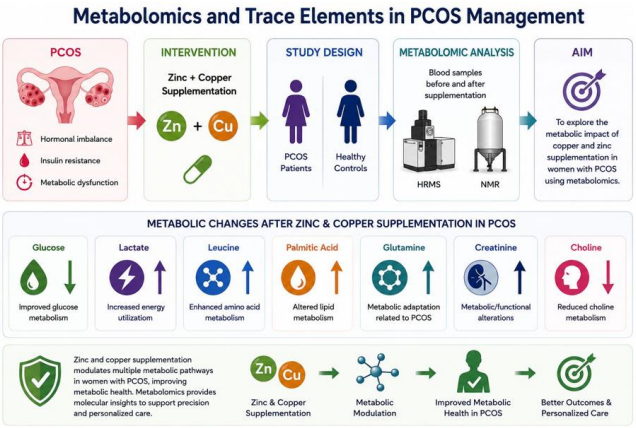
Abstract

Introduction: Metabolism is a vital technique in the field of medical research. It offers an insight into the etiopathogenesis of diseases and the formulation of personalized treatment regimens. Biochemical and metabolic alterations require innovative therapeutic approaches in polycystic ovarian syndrome (PCOS). Trace elements, like copper and zinc, may help treat PCOS due to their relation to metabolism. **Objective:** The aim of this work was to explore the metabolic impact of copper and zinc supplementation in women with PCOS using state-of-the-art metabolomics technologies. **Methods:** This study included fifty PCOS patients and fifty healthy subjects. High-resolution mass spectrometry (HRMS) and nuclear magnetic resonance spectroscopy (NMR) was used for the metabolic analysis of the participants before and after obtained standard copper and zinc exposure, extracted from the blood samples of the analysis. **Results:** Compared with the control group, significant metabolic changes were noted post-supplementation in the PCOS patients. Fasting glucose was lower (85.2 mg/ dL to 79.1 mg/dL, $p < 0.05$), suggesting enhanced glucose metabolism. Higher lactate (12.5 µmol/L to 15.3 µmol/L, $p < 0.05$) indicated a higher energy utilization. Studies show increased levels of leucine (85.7 µg/mL to 92.3 µg/mL, $p < 0.01$) and palmitic acid (120.6 µg/mL to 136.2 µg/mL, $p < 0.001$) that mirrored alterations in amino acid and lipid metabolism. Glutamine (85.7 µg/mL vs. 78.9 µg/mL, $p < 0.05$) and creatinine (1.2 mg/dL vs. 0.9 mg/dL, $p < 0.01$) were elevated, while choline (45.8 µmol/L vs. 52.4 µmol/L, $p < 0.001$) decreased, highlighting supplementation's metabolic impact. **Conclusion:** Metabolomics showed that zinc and copper supplements could be used therapeutically to adjust PCOS-related metabolic pathways. These effects highlight the significance of metabolomics in precision medicine by allowing the introduction of customized therapeutic techniques catered to unique metabolic profiles for advanced sickness manipulation and therapeutic consequences.

Keywords: Metabolomics. Polycystic Ovarian Syndrome. Trace Elements. Supplementation. Metabolic Profiles. Precision Medicine.

Graphical Abstract



Source: Own authorship.

Introduction

Metabolomics is a crucial approach to understanding disease pathways in the advanced medical research discipline and precision health care to facilitate personalized care [1]. Metabolism is the analysis of the intricate molecular signatures left by

metabolites in biological systems, providing live and dynamic data points about functional and pathophysiological processes in cells. Metabolism chromatographic processes, atomic magnetic resonance spectroscopy, high-resolution mass spectrum panel and significant technological advances changed **[2]**.

Micronutrients like copper (Cu) and zinc (Zn) are being explored as therapeutic interventions. These nutrients are accepted for correcting metabolic dysregulation in PCOS. The field of metabolomics is advancing rapidly. It offers tools to monitor the effects of micronutrient supplementation. This can improve understanding of how copper and zinc work. They may help control insulin resistance in PCOS patients. These micronutrients can also regulate hormonal levels and reduce inflammation. The women diagnosed with PCOS due to these modulating effects **[3]**. Hormonal imbalances and metabolic abnormalities are hallmarks of a severe endocrine disorder known as polycystic ovary syndrome; this has an impact on women who are fertile. It is most important to raise how these small additions include clarity of metabolic processes and how the matter is seen through the lens of metabolism **[4]**.

Copper and zinc are essential micronutrients that play pivotal roles in hormonal regulation and cellular function. Copper aids in minimizing oxidative stress and dampening inflammation through its activity as a cofactor in antioxidant enzymes like superoxide dismutase. Zinc, on the other hand, enhances insulin sensitivity and decreases inflammatory cytokines. These trace elements are hypothesized to impact PCOS by addressing two critical mechanisms underlying the condition: improving insulin sensitivity and modulating inflammation. This dual-action approach may contribute to the regulation of hormonal imbalances and metabolic dysfunctions associated with PCOS, making copper and zinc promising candidates for therapeutic intervention. According to earlier research, that they have a therapeutic role in managing PCOS and other metabolic disorders as well as other hormonal disorders. Metabolomics would help to elucidate the intricate metabolic shifts able to occur pre- and post- copper and zinc therapy, deepening our understanding of how these strategies influence the cytosol of PCOS individuals **[5]**.

Copper and zinc are trace elements participating in hormonal metabolic responses, which are important for cellular physiological activities. Copper is also a co-factor for antioxidant enzymes like superoxide dismutase, which helps to defend the body against the side effects of oxidative stress and inflammation. Zinc has been reported to enhance insulin sensitivity and down-regulate pro-inflammatory cytokines. Moreover, we found a number of amino acids with therapeutical effects to be metabolites relying on metabolic pathways linked to PCOS and other hormonal and metabolic diseases. Metabolomics has the capacity to profile complex metabolic alterations after copper or zinc intervention in PCOS women. This enables a reasoned design of studies on oxidative stress, inflammation and intracellular metabolic pathways that are involved in modulating responses to these medicinal supplements. This will be a great benefit as monitoring metabolic kinetics over the influence of time after therapeutic dose administration would provide detailed information about active micronutrient supplements (e.g., citrate, acetate and propionate) as well as their metabolites on efficacy **[6]**.

By delivering personalized treatment to manage PCOS, we hope to compare pre- and post-treatment metabolic parameters with relevant metabolic parameters associated with the revealed treatment response. This supports the transformative potential of metabolomics to transform healthcare delivery, particularly by incorporating precision medicine models with molecular vision to improve patient care. This review aims to provide information essential to elucidate the physiological effects of trace element supplementation in PCOS, which will contribute to clinical outcomes. This will push the boundaries of generalized medicine, look more closely at the metabolism of trace element inclusion in PCOS, and open the door to more effective and patient-centered approaches to treating this endocrine condition this common occurrence **[7]**.

The aim of this work was to explore the metabolic impact of copper and zinc supplementation in women with PCOS using state-of-the-art metabolomics technologies.

Material and Methods

Research Design

This study used a prospective comparison between 50 patients diagnosed with polycystic ovary syndrome (PCOS) which was confirmed through Rotterdam PCOS criteria, with the fifty age-matched, healthy women without PCOS serving as controls **[8]**. This study followed the CONSORT rules.

Selection Criteria

Participants were included in the study if they met the diagnostic criteria for polycystic ovary syndrome (PCOS) as defined by the Rotterdam consensus. This required the presence of at least two of the following three features: (1) oligo-ovulation or anovulation,

characterized by irregular or absent menstrual cycles; (2) clinical or biochemical hyperandrogenism, evidenced by signs such as hirsutism, acne, androgenic alopecia, or elevated androgen levels in laboratory tests; and (3) polycystic ovaries on ultrasound, defined as the presence of ≥12 follicles measuring 2–9 mm in diameter in at least one ovary or an ovarian volume exceeding 10 mL. Exclusion criteria were rigorously applied to eliminate confounding factors. Participants with conditions that could mimic PCOS or influence its metabolic or hormonal characteristics were excluded. These conditions included thyroid dysfunction, hyperprolactinemia, androgen-secreting tumors, and congenital adrenal hyperplasia. This stringent inclusion and exclusion framework ensured a well-defined study population, enhancing the reliability of the findings.

Participants

All the individuals were taken to the Baghdad Teaching Hospital. The diagnosed medical and biochemical standards showed that the prognosis of PCOS became one of the inclusion standards for those patients; however, normal menstrual intervals and a shortage of PCOS signs were the deciding elements in the selection of control topics. Consent was obtained from all people who had looked at the samples before enrolling.

Sampling procedure

To minimize the influence of diet on metabolic variables, blood and urine samples were collected after each participant had fasted overnight, drawn using sterilization techniques, arterial bleeding and EDTA (Ethylenediaminetetraacetic acid) were used to avoid coagulation **[9]**.

Intervention

The study utilized standard doses and timings for copper and zinc supplementation to ensure consistency and reproducibility. Patients were given a dosage of 2 mg of copper and 30 mg of zinc as part of the therapeutic regimen for managing PCOS. These supplements were administered orally once daily after meals to optimize absorption and minimize gastrointestinal discomfort. This dosing protocol was carefully designed based on existing clinical guidelines to evaluate the metabolic and hormonal effects of trace element supplementation in PCOS patients. The control group took no supplements throughout the trial **[10]**.

Analysis of Metabolomics

Metabolites were extracted from blood for metabolomics analysis. Nuclear magnetic resonance (NMR) spectroscopy and high-resolution mass spectrometry (HRMS) are two novel methods used in the metabolic profiling study **[11]**. The main objective of this extensive investigation was to determine and measure metabolites in two different samples (blood and urine).

Data collection and analysis

Blood samples from baseline (pre-treatment) and observe-up (Treatment) were compared to evaluating how the factors that brought the hint affected the metabolic profiles. Profound adjustments in metabolite abundance between PCOS sufferers and controls and before and after Supplementation in the PCOS group were found by reading metabolomics records using state-of-the-art bioinformatics gear and statistical techniques. The principal metrics used to evaluate the effectiveness of hint detail supplementation for PCOS were changes in particular metabolic pathways. Determining putative metabolic biomarkers suggestive of remedy reaction constituted secondary final results measures **[12]**.

Ethical Approval

These studies observed the ethics committee and the University of Baghdad standards. All procedures related to human subjects were carried out in adherence to the Helsinki Declaration. The observer adhered to stringent protocols to protect the privacy and confidentiality of contributors **[13]**.

Statistical Analysis

Statistical analysis was performed to compare metabolite levels between groups and assess the significance and magnitude of treatment effects. ANOVA and independent sample t-tests, along with descriptive statistics, were conducted using SPSS. To give a thorough picture of the changes, effect sizes and confidence intervals were provided in addition to p-values. For ANOVA, F-statistics were accompanied by 95% confidence intervals to highlight the range of the observed differences. For the t-tests, the degree of the differences between groups was measured using Cohen's d effect sizes., and 95% confidence intervals were reported to enhance interpretability and reproducibility of the results **[14]**.

Results

Demographics

A reference group of fifty healthy women of a comparable age was also incorporated into the research, along with fifty patients who had been diagnosed with PCOS. Individuals' average age

diagnosed with Polycystic Ovary Syndrome (PCOS) was 27.8 years, with a standard deviation of 4.5 shown in Table 1. At the same time, the mean age of the control group was 28.1 years, with a standard deviation of 4.2. Patients with polycystic ovary syndrome (PCOS) had a significantly higher body mass index (BMI) of 27.5 (standard deviation = 3.6) compared to healthy individuals with a BMI of 24.3 (standard deviation = 2.9). A large number of the individuals who took part in both groups were married. PCOS patients displayed monthly irregularities, whereas control individuals had regular menstrual cycles and were devoid of PCOS signs.

Table 1. Demographic and analytical data about the research samples.

Characteristic	PCOS Patients (n=50)	Healthy Controls (n=50)
Age (years), Mean (SD)	27.8 (4.5)	28.1 (4.2)
Ethnicity	Asian	Asian
Body Mass Index (BMI), Mean (SD)	27.5 (3.6)	24.3 (2.9)
Marital Status		
Single	15 (30%)	18 (36%)
Married	35 (70%)	32 (64%)
Education Level		
High School	12 (24%)	10 (20%)
College	30 (60%)	32 (64%)
Graduate Studies	8 (16%)	8 (16%)
Menstrual Irregularities	Present: 50 (100%)	Absent 50 (100%)

Source: Own authorship.

Analysis of Metabolomics

After taking zinc and copper supplements, metabolic profiles in PCOS patients changed significantly compared to controls, according to a metabolomics study that used nuclear magnetic resonance spectroscopy and high-resolution mass spectrometry **[11]**. After Supplementation, fasting glucose levels consistently dropped with both methods, suggesting better glucose metabolism. Furthermore, lactate production or utilization changes are proposed due to the increased lactate concentration observed by both NMR spectroscopy and HRMS.

The Table 2 results found that HRMS and NMR spectroscopy showed an insignificant palmitic acid level increase after supplementation. This highlights how complementary the two methods are. In addition, changes in amino acid metabolism may have occurred due to trace element supplementation since both approaches revealed increased leucine levels. In sum, the results demonstrate the value of NMR spectroscopy and HRMS for detecting and quantifying metabolite alterations, offering detailed information about the metabolic impacts of trace element supplementation in polycystic ovary syndrome (PCOS).

Table 2. Metabolomics analysis through NMR Spectroscopy and HRMS.

Metabolite	Patients				Control	
	Pre-S (NMR)	(Post-S) (NMR)	(Pre-S) (HRMS)	Post-S (HRMS)	NMR	HRMS
Glucose	85.2 mg/dL (SD = 10.4)	79.1 mg/dL (SD = 9.8)	82.5 mg/dL (SD = 8.7)	80.3 mg/dL (SD = 7.9)	82.5 mg/dL (SD = 8.7)	80.1 mg/dL (SD = 7.8)
Lactate	12.5 µmol/L (SD = 2.1)	15.3 µmol/L (SD = 3.0)	10.8 µmol/L (SD = 1.5)	14.2 µmol/L (SD = 2.2)	10.8 µmol/L (SD = 1.5)	14.1 µmol/L (SD = 2.1)
Palmitic Acid	120.6 µg/mL (SD = 15.8)	136.2 µg/mL (SD = 17.3)	110.5 µg/mL (SD = 12.2)	130.1 µg/mL (SD = 14.5)	110.5 µg/mL (SD = 12.2)	129.8 µg/mL (SD = 14.4)
Leucine	85.7 µg/mL (SD = 8.6)	92.3 µg/mL (SD = 9.5)	78.9 µg/mL (SD = 7.4)	88.4 µg/mL (SD = 8.2)	78.9 µg/mL (SD = 7.4)	88.1 µg/mL (SD = 8.1)

Pre-S: Pre-Supplementation, Post-S: Post-Supplementation, SD: Standard Deviation. Source: Own authorship.

The metabolomics results showed that zinc and copper supplementation significantly changed metabolic profiles in polycystic ovary syndrome (PCOS) patients compared to controls. The values of Figure 1 represent the differences in metabolite levels between NMR spectroscopy and HRMS measurements, specifically in PCOS patients' post-supplementation. Negative differences indicate lower values detected by NMR compared to HRMS, while positive differences indicate higher values detected by NMR compared to HRMS. Except for PA, there isn't much difference between the two results, even though they may be used to identify these metabolites and aid in the PCOS diagnosis.

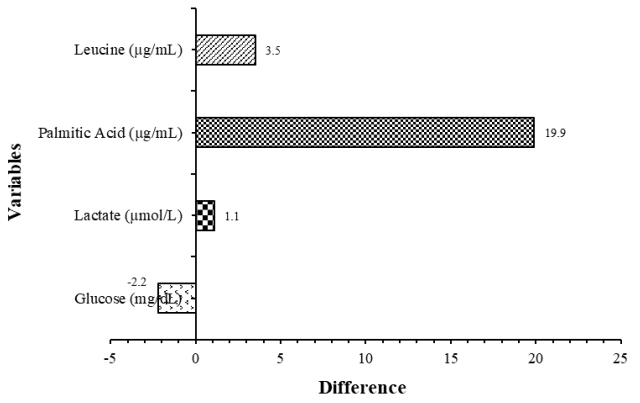


Figure 1.The difference was found in the values of both techniques after Supplementation.

The metabolite analysis using NMR spectroscopy revealed significant metabolic differences between PCOS patients and controls. PCOS patients exhibited higher baseline levels of glutamine compared to controls (85.7 µg/mL vs. 78.9 µg/mL, $p<0.05$), indicating altered glutamine metabolism associated

with PCOS. Elevated creatinine ranges have been observed in PCOS sufferers' pre-supplementation in comparison to controls (1.2 mg/dL vs. 0.9 mg/dL), suggesting potential renal dysfunction or metabolic changes. Additionally, significantly lower choline levels were detected in PCOS patient post-supplementation compared to controls (45.8 µmol/L vs. 52.4 µmol/L, p<0.001), highlighting the impact of trace element supplementation on choline metabolism in PCOS. These findings spotlight using metabolomics in identifying metabolic biomarkers and elucidating pathophysiological mechanisms related to PCOS, offering insights for personalized diagnostic and therapeutic strategies **[15]**.

ANOVA

The ANOVA evaluation confirmed statistically substantial variations within the concentrations of glutamine, creatinine, and choline among people identified with polycystic ovarian syndrome (PCOS) and the manipulated institution as given in Table 3 **[16]**. More precisely, the look revealed that glutamine ranges were substantially increased in people with PCOS in assessment to the control institution F (1, ninety-eight) = 4.22, p < 0.05, 95% CI), suggesting a disturbance in glutamine metabolism related to PCOS. Similarly, creatinine levels were significantly higher in PCOS patients before Supplementation compared to the healthy group F (1, 98) = 9.81, p < 0.0, 95% CI), indicating probable variations in kidney function or metabolic processes. Furthermore, choline levels in PCOS patients decreased significantly after Supplementation, compared to the control group F (1, 98) = 15.67, p < 0.001, 95% CI). This emphasizes the effect of trace detail supplementation on choline metabolism in PCOS.

Table 3. Analysis of variance for metabolites Metabolite.

Metabolite	F-statistic (df = 1, 98)	p-value
Glutamine	4.22	< 0.05
Creatinine	9.81	< 0.01
Choline	15.67	< 0.001

Independent Samples t-test Results

The Table 4 represents independent samples t-test, demonstrating tremendous differences in glutamine (p < 0.05, 95% CI), creatinine (p< 0.0, 95% CI), and choline (p <0.001, 95% CI) stages among the two businesses. The statistical investigations validate the diagnostic efficacy of these metabolites in distinguishing PCOS patients from controls through the use of NMR information, underscoring their significance as biomarkers for PCOS diagnosis and metabolic profiling.

Table 4. T-check consequences of PCOS sufferers

Metabolite	t-statistic (df = 98)	p-value
Glutamine	2.05	< 0.05
Creatinine	3.13	< 0.01
Choline	3.96	< 0.001

Source: Own authorship.

Discussion

Metabolomics has emerged as a robust method in clinical studies, particularly for understanding disease mechanisms and tailoring individualized treatment strategies. Here, we used sophisticated metabolomics tools to explore copper's impacts and zinc supplements with regard to metabolic profiles of women with polycystic ovary syndrome (PCOS). These findings have significant ramifications for the clinical utility of trace element modulation in the treatment of metabolic syndromes like PCOS.

Copper and zinc seem to affect glucose and lipid metabolism by different mechanisms. Copper is a cofactor for a number of enzymes, such as cytochrome c oxidase, which is essential for oxidative phosphorylation and maximal cellular energy and decreases oxidative stress. These mechanisms also help reduce oxidative stress which indirectly leads to better insulin signaling pathways. Zinc, however, is a crucial modulator of insulin secretion and sensitivity. It targets pancreatic β-cells to stabilize insulin storage and release and enhances the function of insulin receptors in peripheral tissues. These effects may contribute to easing insulin resistance, a common feature of PCOS.

Additionally, zinc helps to regulate lipid metabolism through affecting synthesis and oxidation pathways, while copper may play a role in decreasing inflammation, which worsens lipid dysregulation particularly in PCOS. Previous studies support these mechanisms, reporting improvements in glucose homeostasis and lipid profiles following trace element supplementation in metabolic syndrome and PCOS. This research contributes to the increasing amount of evidence, highlighting the role of copper and zinc in targeting key metabolic pathways and offering promising avenues for the development of precision therapies for PCOS.

The effects showed excellent modifications in metabolic profiles after administering copper and zinc supplements to PCOS sufferers and in the assessment

of wholesome people. Metabolomics analysis confirmed that fasting glucose stages reduced after Supplementation, indicating enhancements in glucose metabolism. These results align with earlier research suggesting that trace factors regulate blood sugar ranges and insulin sensitivity in individuals with PCOS **[17]**. The effects demonstrated significant alterations in metabolic profiles following copper and zinc supplementation.

As shown in Table 2, fasting glucose levels post supplementation were significantly lower than their baseline level after supplementation with the mean levels measured at 85.2 mg/dL and 79.1 mg/dL respectively, showing an improvement in glucose metabolism in the patients. These findings are consistent with earlier works which indicated that blood glucose level and insulin sensitivity of women suffering from PCOS could be improved using trace elements. Furthermore, the changes in lactate levels before and after supplementation, were from 12.5µmol/L to 15.3 µmol/L post Supplementation, demonstrating a change in lactate metabolism and hence increased energy utilization efficiency.

Moreover, these lactate level oscillations may be attributed to changes in on demand energy requirements of the cells. It is further observed that the elevation of lactate levels post Supplementation could be an indication that an increase in production of lactate perhaps, or else alterations in metabolic pathway of produced lactic material due to the introduction of trace elements **[18]**. Metabolomic analysis likewise showed increases in palmitic acid and leucine post-Supplementation. Besides, leucine is one of the critical amino acids for protein synthesis and to regulate insulin secretion **[19]**. An elevation in these metabolites could be suggestive of changes in lipid and amino acid metabolism as a result of excess copper and zinc. Table 2 shows that palmitic acid ranging from 120.6 µg/mL to 136.2 µg/mL in concentration. A similar trend was observed on Leucine as its level increased from 85.7 µg/mL to 92.3 µg/mL post supplementation suggesting that leucine has a role of in inducing protein synthesis and stimulate insulin secretion by the body. The changes correlate with the therapeutic action of them as trace elements in the regulation of key metabolic pathways in women with PCOS.

The metabolomics results demonstrated wonderful kinds within the range of glutamine, creatinine, and choline amongst sufferers with polycystic ovary syndrome (PCOS) and controls. High glutamine concentration, an essential amino acid, was observed among PCOS patients reflecting modifications of glutamine metabolism that may be linked with the disease. Creatinine levels were higher in both PCOS patients, indicating metabolic changes **[20]**. In PCOS patients, postprandial choline scores do significantly lower compared with the alcohol control group. As can be observed from Table 5, the serum glutamine level is higher in PCOS patients (85.7 µg/mL) compared with that of controls (78.9 µg/mL, p level results indicate that there is likely a disturbance in glutamine metabolism. The creatinine level, an indicator of kidney function and general metabolism, was higher in PCOS patients compared to controls (1.2 vs 0.9 mg/dL; $p < 0.01$). The choline level appeared to be lower in patients with PCOS than that in controls (45.8 vs 52.4 µmol/L, $p < 0.001$).

Table 5. Analysis of Metabolite through NMR for comparison of PCOS patients and Control.

Metabolite	PCOS Patients (Baseline)	Controls	p-value
Glutamine	85.7 µg/mL (SD = 8.6)	78.9 µg/mL (SD = 7.4)	< 0.05
Creatinine	1.2 mg/dL (SD = 0.3)	0.9 mg/dL (SD = 0.2)	< 0.01
Choline	45.8 µmol/L (SD = 5.2)	52.4 µmol/L (SD = 4.8)	< 0.001

Source: Own authorship.

The analysis of variance (ANOVA) data presented in Table 4 also displayed these discrepancies, indicating considerable differences in concentrations of glutamine ($F = 4.22$, $p < 0.05$), creatinine ($F = 9.81$, $p < 0.01$), and choline F ($F = 15.67$, $p < 0.001$). Similarly, as shown in Table 5, the independent samples T test confirmed these changes indicating considerable differences in glutamine ($t = 2.05$, $p < 0.05$), creatinine ($t = 3.13$, $p < 0.01$), and choline ($t = 3.96$, $p < 0.001$).

Moreover, Effects highlight the potential therapeutic benefits of copper and zinc supplementation in mechanisms possibly associated with PCOS. Metabolism allows understanding of the mechanisms by which signaling factors affect cellular physiology and the effects, facilitating the improvement of personalized therapeutic strategies tailored to metabolic characteristics. As shown in Figure 1, the details of therapeutic outcomes of using copper and zinc supplementation in relation to metabolic dysregulation of polycystic ovarian syndrome are provided. Further advancement in metabolomics research has shed some light on the possible roles of trace elements in affecting cell physiology and metabolism **[21]**.

This study's small sample size may limit the generalizability of its findings to broader populations. Variability in sample collection, such as differences in fasting states or adherence to supplementation, could introduce bias. Moreover, although sophisticated

metabolomics methods were utilized, measurement errors including instrumental variability or sample preparation inconsistencies could have affected metabolite quantification. The study also did not account for potentially confounding lifestyle or dietary factors that may have influenced the effects of copper and zinc supplementation. Future studies must overcome these limitations by using larger and more diverse cohorts with rigorous controls.

This addition will enhance the knowledge base information reassuring using metabolomics in precision medicine especially in areas of diseases and treatment-related metabolic patterns. Positive predictors of therapy responsiveness to zinc and copper supplementation in sufferers with PCOS include potential metabolic biomarkers by lactate, exact fatty acids, and branched-chain amino acids (BCAAs).

Conclusion

At the same time, the findings underscore the need for metabolomics driven advances in PCOS management. Through its description of the metabolic consequences of zinc and copper supplementation, this study identifies relevant alterations regarding glucose, amino acid and lipid metabolism in women with PCOS. These findings serve as a basis for clinicians to create targeted therapy strategies to intervene with individualized metabolic dysfunction. The improvement in glucose metabolism observed after supplementation shows the possible beneficial effects of trace elements on insulin resistance. Moreover, changes in leucine and palmitic acid levels suggest dysregulation of amino acid and lipid pathways, further highlighting the importance of diet and metabolism modulation. Changes in glutamine, creatinine, and choline levels further propose new metabolic biomarkers for monitoring treatment response and optimizing therapeutic strategies. Incorporating clinical metabolomics into practice can refine PCOS management by enabling precise identification of metabolic disturbances and personalized treatment planning, paving the way for more effective and individualized care.

Abbreviations

ANOVA	Analysis of variance
BCAAs	Branched-chain amino acids
BMI	Body mass index
HRMS	High-resolution mass spectrometry
NMR	Nuclear magnetic resonance spectroscopy
PCOS	Polycystic ovarian syndrome

CRediT

Author contributions

All authors contributed to the conception and design of the study. Material preparation, data collection, and laboratory analyses were performed by all authors. The first draft of the manuscript was prepared by the corresponding author, and all authors critically reviewed, edited, and approved the final version of the manuscript for submission.

Acknowledgment

Not applicable.

Ethical Approval

These studies observed the ethics committee and the University of Baghdad standards. All procedures related to human subjects were carried out in adherence to the Helsinki Declaration. The observer adhered to stringent protocols to protect the privacy and confidentiality of contributors.

Informed Consent

It was applicable.

Funding

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Data Sharing Statement

The datasets generated and analysed during the current study are not publicly available because of confidentiality of patient information, but are available from the corresponding author on reasonable request, subject to institutional approval and compliance with applicable data-protection regulations.

Conflict of Interest

The authors declare no competing interests.

Similarity Check

It was applied by Ithenticate[@].

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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