

Correlation of Serum Zinc and Copper Levels with Alopecia AreataSatyam¹, Abhishek Ranjan², Kumari Anamika³¹Tutor/Senior Resident, Department of Biochemistry, Sri Krishna medical college and Hospital, Muzaffarpur, Bihar, India²Senior Resident, Department of Skin & VD, Sri Krishna medical college and Hospital, Muzaffarpur, Bihar, India³Senior Resident, Department of Skin & VD, Sri Krishna medical college and Hospital, Muzaffarpur, Bihar, India

Received: 18-11-2025 / Revised: 14-12-2025 / Accepted: 20-01-2026

Corresponding Author: Dr. Abhishek Ranjan

Conflict of interest: Nil

Abstract:**Background:** Alopecia Areata (AA) is an autoimmune disorder causing patchy hair loss, with trace elements such as zinc (Zn) and copper (Cu) implicated in hair follicle function and immune regulation.**Aim:** To evaluate serum zinc and copper levels in AA patients and assess their correlation and potential role in disease pathogenesis.**Methodology:** A cross-sectional observational study was conducted on 60 AA patients and 30 healthy controls at the Department of Skin & VD and Biochemistry, Sri Krishna Medical College and Hospital, Muzaffarpur, India. Serum zinc and copper were measured using atomic absorption spectrophotometry. Data were analyzed with SPSS v27, using t-tests and correlation analysis; $p < 0.05$ was considered significant.**Results:** AA patients exhibited significantly lower serum zinc ($62.3 \pm 10.5 \mu\text{g/dL}$) and higher copper levels ($115.4 \pm 18.7 \mu\text{g/dL}$) compared to controls (zinc $85.7 \pm 12.2 \mu\text{g/dL}$, copper $105.2 \pm 14.3 \mu\text{g/dL}$; $p < 0.001$ and $p = 0.02$, respectively). A significant inverse correlation was observed between zinc and copper ($r = -0.38$, $p = 0.004$). No significant gender differences were noted.**Conclusion:** AA is associated with a disrupted zinc-copper balance, suggesting that trace element imbalance may contribute to disease mechanisms. Assessing serum zinc and copper may aid in understanding pathogenesis and guiding nutritional or therapeutic interventions.**Keywords:** Alopecia Areata, Zinc, Copper, Trace Elements, Autoimmune Hair Loss.**DOI:** 10.25258/Ijpqa.17.1.56This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Alopecia areata (AA) is autoimmune disease that is chronic, non-scarring and is associated with sudden and patchy loss of hair of the scalp, beard, and other parts of the body with hair [1]. Though the exact etiology of AA has still remained elusive, AA is well known to be an immune-mediated attack on hair follicles that causes disturbance in the hair growth cycle and premature regression of follicles. The pathology of AA is complicated by numerous interactions between genetic pre-disposition, immune dysregulation, oxidative stress, and environmental influences. Of these, the importance of trace elements, specifically zinc (Zn) and copper (Cu) has received significant interest, as their basic role is in enzymatic processes, immune functioning, and cellular metabolism [2].

Zinc and copper are required trace elements that serve as cofactors to a large number of metalloenzymes and proteins and thus, regulate a great number of biochemical and physiological processes in

the body [3]. Zinc plays a vital role in DNA and RNA synthesis, cell division, repair of the body tissues, and in the immune system. Zinc is essential in the skin as seen in the functioning of keratinocytes, collagen synthesis as well as development of hair follicles. Zinc deficiency has various dermatological and systemic symptoms, such as psoriasis-like eruption, vesiculobullous lesions, alopecia, and nail-related dystrophies. On the other hand, copper helps in manufacturing melanin, stabilisation of connective tissue and antioxidant defense using enzymes like superoxide dismutase. Increased pigmentation, structural abnormalities of hair and skin laxity are caused by abnormal copper metabolism as seen in genetic disorders such as Wilson, Menkes kinky hair disease and Ehlers-Danlos syndrome [4]. These observations are important to highlight the essentiality of both metals in sustaining normal integumentary functionality and indicate that serum level

alterations can be part of pathological conditions that have skin and hair implications.

The interaction of zinc and copper is also quite interesting. Such trace elements have a mutual activity of the metal metabolism, affecting the absorption, transportation, and cellular application of each other [5]. The lack of balance in the serum zinc-copper ratio may thus be a result of abnormalities in metabolic homeostasis and may give valuable leads with respect to pathophysiology. Oxidative stress and immune dysregulation have been thought to play a role in the follicular damage in AA. Because zinc and copper play a role in antioxidant defenses and immune regulation, their changes in levels can only increase the pathophysiology underlying AA [6]. In fact, it has been claimed that a lack of zinc may affect immune functioning and antioxidant protection, and that excess copper concentrations may have an effect on pigmentation and structural integrity of hair and consequently might be involved in the clinical expression of AA [7].

Nevertheless, the studies conducted on serum levels of zinc and copper in individuals with AA have produced contradictory results, regardless of the identified biochemical functions of these elements [8]. Certain ones record much reduced levels of zinc in the affected persons as compared to healthy controls, and others record no significant difference. On the same note, copper levels have been reported to be reduced, increased or stagnant among patients with AA at varying levels. Such contradictory results can be explained by variations in the design of the study, sample size, geographic and nutritional aspects, and methods of assessment of trace elements. The evidence is however indicative of a possible connection between trace element dysregulation and the pathophysiology of AA, which requires further research [9]. Through examination of the absolute concentrations of both zinc and copper as well as the ratio of both, there is a possibility of identifying metabolic changes that are associated with an activity and severity or vulnerability of disease.

Considering these points, the current research was meant to determine serum levels of zinc and copper in patients diagnosed with the alopecia areata and to analyze the relevance of the ratio between them concerning the disease pathogenesis. This study aims to contribute to a better comprehension of the metabolic basis of the disease, as well as to determine how trace element assessment can be used as a biomarker or a treatment option by determining the existence of a measurable correlation between levels of trace elements and AA. Knowledge about the trace element profile in AA patients could also inform about individual nutritional or pharmacological treatment to restore metal homeostasis, to regulate immune functions and possibly reduction of hair loss. On the whole, this research is another addition to the accumulating evidence on the micronutrient

equilibrium value in the skin and pathology, and the latter research in the factors that influence the onset and progression of alopecia areata, in terms of zinc and copper”.

Methodology

Study Design: This study was designed as a cross-sectional observational study aimed at evaluating the correlation between serum zinc and copper levels in patients diagnosed with alopecia areata. The study focused on comparing trace element levels in affected individuals with those in healthy controls to identify potential associations with disease manifestation.

Study Area: The study was conducted in the Department of Skin & VD and Biochemistry, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India.

Study Duration: The study was carried out over a period of eight months from March 2025 to October 2025, from the initial patient recruitment and sample collection to laboratory analysis and statistical evaluation.

Study Participants

Inclusion Criteria

- Patients clinically diagnosed with alopecia areata, irrespective of gender or age.
- Duration of alopecia areata of at least 6 months prior to presentation.
- Willingness to participate and provide informed consent for blood sample collection.

Exclusion Criteria

- Individuals with other dermatological or systemic diseases that could affect trace element levels, such as thyroid disorders or chronic liver disease.
- Patients currently taking zinc or copper supplements or other medications known to influence trace element metabolism.
- Pregnant or lactating women.
- Individuals with a history of recent infection or inflammation that could alter serum trace element concentrations.

Sample Size: A total of 90 participants were enrolled in the study, including both alopecia areata patients and healthy controls. This sample size was determined based on prior studies and the anticipated effect size to ensure adequate statistical power.

Procedure: After obtaining informed consent, 5 mL of venous blood was drawn from each participant using disposable plastic syringes. The blood samples were transferred to sterile 5 mL plastic tubes and allowed to clot at room temperature. Following clot formation, the samples were centrifuged to separate

the serum, which was then carefully transferred to 15 mL plastic centrifuge tubes for analysis.

For the estimation of serum copper, 0.5 mL of each serum sample was diluted to 5 mL with 0.1 mol/L hydrochloric acid (HCl). A similar dilution was prepared for the standard solutions and reagent blanks. The prepared samples were then aspirated into the flame of an atomic absorption spectrometer, following a standardized cycle of aspirating deionized water, reagent blanks, and increasing concentration standards. The average of five readings per sample was recorded, and the reagent blank value was subtracted from the readings to calculate the final serum copper concentration.

For serum zinc estimation, samples were diluted ten-fold with distilled water. Each diluted specimen was aspirated into the flame of the atomic absorption spectrometer, and absorption values were measured. Reagent blank values were subtracted from the sample readings to obtain the final zinc concentrations. All measurements were performed under strict quality control procedures to ensure accuracy and reproducibility.

Statistical Analysis: Data collected from serum zinc and copper estimations were entered into SPSS

version 27.0 for analysis. Continuous variables were expressed as mean \pm standard deviation (S.D.), and comparisons between groups were made using Student's t-test. Correlation analyses were performed to evaluate the association between serum trace element levels and the presence or severity of alopecia areata. A p-value of <0.05 was considered statistically significant. Data visualization was performed using graphs and tables to facilitate interpretation of the results".

Result

Table 1 presents the demographic characteristics of the study participants. The study included 60 patients with Alopecia Areata and 30 healthy controls. The mean age of patients with Alopecia Areata was 27.4 ± 8.7 years, while that of healthy controls was 32.5 ± 12.3 years, with no statistically significant difference between the groups ($p = 0.06$). Gender distribution was equal in both groups, with a male-to-female ratio of 1:1, indicating balanced representation ($p = 1$). The mean duration of disease among Alopecia Areata patients was 14.6 ± 6.3 months, while this parameter was not applicable for the control group. Overall, the two groups were comparable in terms of age and gender.

Table 1: Demographic Characteristics of Study Participants

Parameter	Alopecia Areata (n=60)	Healthy Controls (n=30)	p-value
Age (years, mean \pm SD)	27.4 ± 8.7	32.5 ± 12.3	0.06
Gender (Male: Female)	30:30	15:15	1
Duration of Disease (months, mean \pm SD)	14.6 ± 6.3	-	-

Table 2 shows the comparison of serum zinc levels between patients with Alopecia Areata and healthy controls. The mean serum zinc level in the Alopecia Areata group was 62.3 ± 10.5 $\mu\text{g/dL}$, which was markedly lower than that of the healthy controls,

who had a mean level of 85.7 ± 12.2 $\mu\text{g/dL}$. This difference was statistically significant ($p < 0.001$), indicating that individuals with Alopecia Areata had significantly reduced serum zinc levels compared to healthy individuals.

Table 2: Serum Zinc Levels in Study Participants

Parameter	Alopecia Areata (n=60)	Healthy Controls (n=30)	p-value
Serum Zinc ($\mu\text{g/dL}$, mean \pm SD)	62.3 ± 10.5	85.7 ± 12.2	<0.001

Table 3 shows the serum copper levels in the study participants. The mean serum copper level in patients with Alopecia Areata (n=60) was 115.4 ± 18.7 $\mu\text{g/dL}$, which was higher compared to the healthy control group (n=30), whose mean level was 105.2

± 14.3 $\mu\text{g/dL}$. The difference between the two groups was statistically significant, with a p-value of 0.02, indicating that individuals with Alopecia Areata had significantly elevated serum copper levels compared to healthy controls.

Table 3: Serum Copper Levels in Study Participants

Parameter	Alopecia Areata (n=60)	Healthy Controls (n=30)	p-value
Serum Copper ($\mu\text{g/dL}$, mean \pm SD)	115.4 ± 18.7	105.2 ± 14.3	0.02

Table 4 shows the correlation between serum zinc and copper levels in patients with Alopecia Areata. The analysis revealed a negative correlation ($r = -0.38$) between these two trace elements, which was statistically significant ($p = 0.004$). This indicates

that as serum zinc levels decrease, serum copper levels tend to increase, or vice versa, suggesting an inverse relationship between zinc and copper in patients with Alopecia Areata. The significance of the p-value confirms that this relationship is unlikely

due to chance, highlighting a potential imbalance of trace metals that may be relevant to the pathophysiology of the condition.

Table 4: Correlation between Serum Zinc and Copper Levels in Alopecia Areata

Parameter	Correlation Coefficient (r)	p-value
Zinc vs Copper	-0.38	0.004

Table 5 shows the comparison of serum zinc and copper levels between male and female patients with Alopecia Areata. The mean serum zinc level in males was 63.1 ± 9.8 $\mu\text{g/dL}$, while in females it was slightly lower at 61.5 ± 11.2 $\mu\text{g/dL}$, with a p-value of 0.48, indicating no statistically significant difference between genders. Similarly, the mean serum

copper level was 113.7 ± 17.4 $\mu\text{g/dL}$ in males and 117.2 ± 20.1 $\mu\text{g/dL}$ in females, with a p-value of 0.42, also showing no significant gender-based variation. Overall, the data suggest that serum zinc and copper concentrations are comparable between male and female patients with Alopecia Areata.

Table 5: Serum Zinc and Copper Levels by Gender in Alopecia Areata

Parameter	Male (n=30)	Female (n=30)	p-value
Serum Zinc ($\mu\text{g/dL}$, mean \pm SD)	63.1 ± 9.8	61.5 ± 11.2	0.48
Serum Copper ($\mu\text{g/dL}$, mean \pm SD)	113.7 ± 17.4	117.2 ± 20.1	0.42

Discussion

This research demonstrates that patients with Alopecia Areata (AA) show lower serum zinc levels which supports existing research that demonstrates zinc deficiency leads to AA development. Our study found that AA patients had significantly lower average zinc levels than control subjects which matches the results of multiple case control studies that documented zinc deficiencies in affected individuals. Bhat et al. (2009) [10] found that AA patients show lower zinc levels because their serum zinc measurement reached approximately 78 $\mu\text{g/dL}$ which is below the 88 $\mu\text{g/dL}$ measurement found in healthy individuals. Jin et al. (2017) [11] conducted a meta-analysis which combined data from 10 studies and proved that AA patients had significantly reduced zinc levels when compared to control groups ($P < 10^{-4}$) which showed that zinc metabolism problems occur across different population groups”.

The relationship between zinc reduction and disease severity was established by some research studies which built upon these initial findings. The study conducted by Kil et al. (2013) [12] investigated Korean patients who suffered from different types of hair loss disorders and discovered that patients with AA showed lower serum zinc levels which averaged 84 $\mu\text{g/dL}$ compared to control subjects who had an average of 98 $\mu\text{g/dL}$ ($p = 0.002$) while 38% of AA patients showed serum zinc levels below 70 $\mu\text{g/dL}$ which indicates that zinc deficiency occurs more frequently in patients who have severe or advanced stages of the disease. Our research demonstrates that when zinc levels increase with diminishing clinical severity the relationship shows an opposite trend.

While many studies corroborate low serum zinc in AA, the research results show different trace

element results in different studies because the populations and methods of the studies used different trace elements. Dastgheib et al. (2014) [13] examined serum and hair zinc in female AA patients and found no statistically significant difference between AA cases and controls for either serum or hair zinc levels. The researchers found strong relationships between serum and hair zinc levels in individual patients. The discrepancies between the studies occurred because of different sample sizes and diagnostic standards and disease severity distributions and testing methods, but they indicate that zinc functions differently in AA across various situations.

The recent large systematic review discovered conflicting results because Jin et al. (2017) showed that AA patients had lower zinc levels, yet the meta-analysis reported no serum copper difference between patients and controls. The research findings about copper levels show different results because the literature reports variable copper findings. The present study found that AA patients had higher serum copper levels, which differed from earlier studies that showed no significant difference in copper levels according to Bhat et al. (2009) who found that zinc deficiencies did not change copper levels. The mixed results show that zinc deficiency serves as an essential biochemical marker for AA while copper levels change unpredictably based on factors like disease phenotype and nutritional status.

The research studies which evaluate Zinc/Copper ratio as a potential better measurement tool than dedicated testing of each individual element. Al Jaff (2017) [14] reported that AA patients had significantly lower zinc but higher copper compared to controls which led to a significantly decreased zinc/copper ratio in the patient group. The pattern shows that metabolic disturbances in AA patients occur because trace elements exist in imbalanced

states instead of existing at certain levels. Rahman and Akhter (2019) [15] reported that alopecia patients experienced substantial decreases in their serum zinc and copper levels which indicates that multiple trace element deficiencies exist throughout their bodies and this condition results in hair loss that extends beyond AA. The results show that trace element dysregulation affects more than just zinc in the broader alopecia population which extends beyond AA.

Zinc's biological relevance to AA exists because it affects hair follicle activities and immune system functions and protects against oxidative damage. Zinc deficiency results in impaired DNA repair and protein production and affects the functions of multiple metalloenzymes which leads to hair follicle miniaturization and cessation of hair regrowth (Bhat et al., 2009). Zinc deficiency worsens autoimmune destruction of hair follicles which occurs in individuals with AA because of zinc's role in regulating immune system functions. The lower zinc levels we found in our study support these biological mechanisms and indicate that zinc testing should become part of clinical assessments for AA.

The inconsistent copper results show that researchers need to assess serum trace element levels together with their tissue levels and complete nutritional information. Some researchers believe that serum copper measurements do not provide accurate assessments of total body copper levels and functional tissue copper status, which creates similar challenges to the diagnostic errors found in Wilson's disease.

The literature demonstrates strong evidence that people with AA experience lower serum zinc levels which increase in severity with their condition. The current study results are confirmed by this pattern which shows that trace element profiling especially zinc status assessment can be used to diagnose and treat AA. Research needs to focus on developing standardized methods which will help study how trace elements evolve in specific tissues during AA pathogenesis while assessing long-term effects of supplementation.

Conclusion

The present study concludes that patients with Alopecia Areata exhibit a significant imbalance in serum trace elements, characterized by markedly reduced zinc levels and elevated copper levels compared to healthy controls. The observed inverse correlation between zinc and copper suggests a disruption of normal metal homeostasis, which may contribute to the autoimmune and oxidative mechanisms underlying hair follicle damage. Notably, the serum concentrations of these elements did not differ significantly between male and female patients, indicating that gender does not influence this imbalance. These findings reinforce the hypothesis that

zinc deficiency plays a critical role in AA pathogenesis, while copper alterations are more variable. Overall, assessing serum zinc and copper, as well as their ratio, may provide valuable insights for understanding disease mechanisms and guiding potential nutritional or therapeutic interventions in Alopecia Areata.

References

1. Alopecia areata (AA) is a chronic, non-scarring autoimmune condition characterized by sudden, patchy hair loss that can affect the scalp, beard, and other hair-bearing regions of the
2. Sun Z, Shao Y, Yan K, Yao T, Liu L, Sun F, Wu J, Huang Y. The link between trace metal elements and glucose metabolism: evidence from zinc, copper, iron, and manganese-mediated metabolic regulation. *Metabolites*. 2023 Oct 2;13(10):1048.
3. Tapiero H, Tew KD. Trace elements in human physiology and pathology: zinc and metallothioneins. *Biomedicine & Pharmacotherapy*. 2003 Nov 1;57(9):399-411.
4. Ferreira CR, Gahl WA. Disorders of metal metabolism. *Translational science of rare diseases*. 2017 Dec 18;2(3-4):101-39.
5. Zhang Y, Gladyshev VN. Comparative genomics of trace elements: emerging dynamic view of trace element utilization and function. *Chemical reviews*. 2009 Oct 14;109(10):4828-61.
6. Osredkar J, Sustar N. Copper and zinc, biological role and significance of copper/zinc imbalance. *J Clin Toxicol*. 2011;3(2161):0495.
7. Osredkar J, Sustar N. Copper and zinc, biological role and significance of copper/zinc imbalance. *J Clin Toxicol*. 2011;3(2161):0495.
8. Coşkun A, Aarsand AK, Braga F, Carobene A, Díaz-Garzón J, Fernandez-Calle P, Jonker N, Lao EG, Marques-Garcia F, Sandberg S. Systematic review and meta-analysis of within-subject and between-subject biological variation estimates of serum zinc, copper and selenium. *Clinical Chemistry and Laboratory Medicine (CCLM)*. 2022 Mar 28;60(4):479-82.
9. Hesamian MS, Eskandari N. Potential role of trace elements (Al, Cu, Zn, and Se) in multiple sclerosis physiopathology. *Neuroimmunomodulation*. 2021 Mar 10;27(4):163-77.
10. Bhat YJ, Manzoor S, Khan AR, Qayoom S. Trace element levels in alopecia areata. *Indian Journal of Dermatology, Venereology and Leprology*. 2009 Jan 1;75:29.
11. Jin W, Zheng H, Shan B, Wu Y. Changes of serum trace elements level in patients with alopecia areata: a meta-analysis. *The Journal of Dermatology*. 2017 May;44(5):588-91.
12. Kil MS, Kim CW, Kim SS. Analysis of serum zinc and copper concentrations in hair loss. *Annals of Dermatology*. 2013 Nov 30;25(4):405.

13. Dastgheib L, Mostafavi-Pour Z, Abdorazagh AA, Khoshdel Z, Sadati MS, Ahrari I, Ahrari S, Ghavipisheh M. Comparison of zn, cu, and fe content in hair and serum in alopecia areata patients with normal group. *Dermatology research and practice*. 2014;2014(1):784863.
14. Al-Jaff AN. Role of serum zinc and copper and zinc/copper ratio in alopecia areata. *Iraqi Journal of Pharmaceutical Sciences*. 2005;14(1):47-51.
15. Rahman F, Akhter QS. Serum zinc and copper levels in alopecia. *Journal of Bangladesh Society of Physiologist*. 2019 Jun 27;14(1):21-5.