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Original Article

Role of Trace Elements in Pregnant Women with Malaria: A Case-Control Study

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Abstract

Background: Malaria is a significant public health and socio-economic issue, affecting over 300 million people annually across more than 90 countries. Pregnant women are particularly vulnerable to malaria due to their decreased immunity, which increases the risk of adverse pregnancy outcomes, including low birth weight, preterm delivery, and infant mortality.

Objective: This study aimed to investigate the role of trace elements in pregnant women with vivax malaria by comparing their serum concentrations with those of healthy pregnant women.

Methods: This hospital-based case-control study was conducted at Liaquat University of Medical & Health Sciences and City Hospital, Hyderabad, Sindh, Pakistan. A total of 120 participants were enrolled, comprising 60 pregnant women diagnosed with gestational vivax malaria and 60 age- and gestational age-matched healthy pregnant women. Blood samples were collected and analyzed using Atomic Absorption Spectroscopy to measure serum levels of magnesium (Mg), iron (Fe), copper (Cu), and zinc (Zn). Data were statistically analyzed using SPSS version 25, with significance set at $p < 0.05$.

Results: The study found significantly lower concentrations of copper, magnesium, zinc, and iron in the serum of pregnant women with vivax malaria compared to healthy controls. The mean serum levels for copper were 1.50 ± 0.59 mg/L in the malaria group versus 2.01 ± 0.41 mg/L in controls, magnesium was 1.60 ± 0.72 mg/L versus 2.09 ± 0.87 mg/L, zinc was 0.93 ± 0.63 mg/L versus 1.40 ± 0.57 mg/L, and iron was 0.97 ± 0.82 mg/L versus 1.40 ± 0.77 mg/L ($p < 0.001$ for all comparisons).

Conclusion: The findings suggest that pregnant women with vivax malaria have significant deficiencies in essential trace elements, which may contribute to compromised immune function and adverse pregnancy outcomes. Addressing these deficiencies through targeted nutritional interventions could enhance immunity and improve maternal and neonatal health outcomes in malaria-endemic regions.

1 Introduction

Malaria is a significant public health concern affecting more than 300 million people worldwide every year. It is prevalent in over 90 countries, presenting a major socio-economic challenge, especially in regions with high transmission rates. Transmitted by the bite of female Anopheles mosquitoes, malaria is primarily caused by four species of Plasmodium parasites: Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, and Plasmodium falciparum, with the latter being the most lethal due to its capacity to cause severe disease and high mortality rates (3). In malaria-endemic regions, pregnant women are particularly vulnerable due to decreased immunity, which increases the risk of adverse outcomes such as low birth weight (LBW), stillbirth, spontaneous abortion, and preterm delivery (4, 6, 9). Placental malaria, characterized by the sequestration of parasites in the placenta, is associated with a two-fold increased risk of stillbirth and is responsible for a significant proportion of LBW cases (8, 10). This condition contributes to elevated infant mortality rates, with an estimated 60,000 to 200,000 infant deaths annually attributed to malaria-associated LBW in Africa alone (11).

The role of trace elements in the pathophysiology of malaria is of growing interest. These elements, including magnesium, iron, copper, and zinc, serve as cofactors in numerous enzymatic reactions and are crucial for maintaining immune function. Malaria infection can disrupt the metabolism of these trace elements, leading to deficiencies that may exacerbate the disease's severity (13). For instance, zinc

deficiency is known to impair immune response, potentially increasing susceptibility to malaria (14). Moreover, the malaria parasite's metabolic pathways require various enzyme cofactors, including trace metals, suggesting that deficiencies in these nutrients could affect both the host's immune response and the parasite's survival (15). Previous studies have highlighted the importance of trace elements in modulating oxidative stress and immune function during malaria, with variations in serum levels of these elements observed in infected individuals compared to healthy controls (19, 20, 21).

In Pakistan, malaria remains a persistent health issue, with millions at risk due to inadequate prevention measures and healthcare infrastructure. Gestational malaria, particularly due to Plasmodium vivax, poses significant risks to maternal and fetal health, yet there is limited information on the metabolic alterations occurring in pregnant women with malaria. Understanding the role of trace elements in this context could provide insights into potential therapeutic interventions to improve outcomes for affected women and their infants. This study aims to investigate the concentrations of key trace elements in the blood serum of pregnant women with vivax malaria compared to healthy pregnant controls, exploring the potential implications of these findings for maternal and neonatal health. By examining the metabolic disturbances associated with malaria in pregnancy, this research seeks to contribute to the development of strategies to enhance immunity and mitigate the adverse effects of malaria through targeted nutritional and therapeutic interventions.

2 Material and Methods

This study was a hospital-based case-control study conducted at Liaquat University of Medical & Health Sciences (LUH), Jamshoro, and City Hospital, Hyderabad, Sindh, Pakistan. A total of 120 pregnant women were enrolled, comprising 60 patients diagnosed with gestational vivax malaria and 60 healthy pregnant women as controls. Participants were matched by age and gestational age and were selected using a simple random sampling technique. The inclusion criteria for the malaria group included confirmed cases of Plasmodium vivax malaria diagnosed by blood smear, while the control group consisted of healthy pregnant women with no history of malaria. Women with any other chronic illness or pregnancy-related complications were excluded from the study.

Ethical approval for the study was obtained from the Ethics Committee of Liaquat University of Medical & Health Sciences, Jamshoro. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants after explaining the study's purpose, procedures, and potential risks.

Blood samples were collected from each participant under sterile conditions. A 5 ml venous blood sample was drawn, and the serum was separated by centrifuging at 5000 rpm for 20 minutes. Serum samples were then treated with a 1M solution of sulfosalicylic acid (SSA) and centrifuged again at 5000 rpm for 10 minutes to clarify the solution. The concentrations of magnesium, iron, copper, and zinc in the serum were measured using an atomic absorption spectrophotometer (Varian Atomic Absorption Model A-20). Specific wavelengths were used for each element: 213 nm for zinc, 324 nm for copper, 285 nm for magnesium, and 248 nm for iron.

Commercial trace metal atomic absorption standard solutions (1000 µg/mL) for copper, iron, magnesium, and zinc were used. Working standards were prepared by diluting these stock solutions with deionized water and adding a few drops of concentrated hydrochloric acid. All reagents, including ferrous sulfate, magnesium sulfate, zinc sulfate, and copper sulfate, were of ultra-pure grade and were purchased from Merck Company. Volumetric flasks were meticulously cleaned with 1% nitric acid and rinsed with deionized water to ensure the accuracy of measurements.

Demographic data and clinical characteristics of participants were collected through structured interviews and medical records. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables were expressed as mean ± standard deviation (SD), and comparisons between groups were made using the student's t-test. A p-value of less than 0.05 was considered statistically significant.

The study aimed to elucidate the role of trace elements in pregnant women with malaria, providing insights into potential nutritional and therapeutic interventions to improve maternal and neonatal outcomes.

3 Results

The study investigated the concentrations of trace elements in the serum of pregnant women with vivax malaria compared to healthy pregnant controls. The findings are presented in two tables, detailing the mean concentrations of trace elements and the demographic profiles of the study participants.

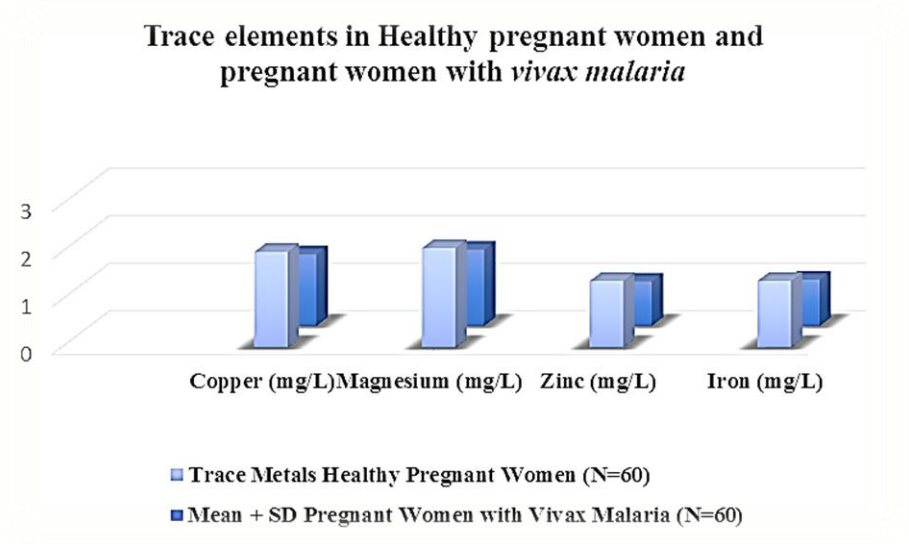
Trace Element Concentrations

The concentrations of copper, magnesium, zinc, and iron in the serum were significantly lower in pregnant women with vivax malaria than in the healthy control group. The results are summarized in Table 1.

Table 1. Mean ± SD of Trace Elements in Pregnant Women

Trace Element	Healthy Pregnant Women (mg/L)	Pregnant Women with Vivax Malaria (mg/L)	P-value
Copper	2.01 ± 0.41	1.50 ± 0.59	<0.001
Magnesium	2.09 ± 0.87	1.60 ± 0.72	<0.001
Zinc	1.40 ± 0.57	0.93 ± 0.63	<0.001
Iron	1.40 ± 0.77	0.97 ± 0.82	<0.001

The results indicate a significant reduction in the serum levels of copper, magnesium, zinc, and iron in pregnant women with malaria compared to healthy pregnant women ($p < 0.001$ for all trace elements). These deficiencies may suggest impaired metabolic and immune functions in malaria-infected pregnant women, potentially contributing to adverse pregnancy outcomes.



Demographic Profiles

The demographic characteristics of the study participants are presented in Table 2. Pregnant women with vivax malaria had significantly lower hemoglobin levels and were of higher parity and gestational age compared to the control group. The age of the participants was also higher in the malaria group. Data show that pregnant women with vivax malaria were older and had a higher number of pregnancies and more advanced gestational age than the control group. Additionally, the significantly lower hemoglobin levels in the malaria group indicate an anemic condition, which is common in malaria-infected individuals and can exacerbate complications during pregnancy

Table 2. Demographic Profiles of Participants

Parameter	Healthy Pregnant Women	Pregnant Women with Malaria	P-value
Hemoglobin (g/dL)	11.2 ± 1.15	7.1 ± 1.12	<0.05
Parity	1.2 ± 1.3	2.9 ± 2.56	<0.05
Gestational Age (weeks)	20 ± 2.23	26 ± 2.56	<0.05
Age (years)	26.2 ± 3.64	33.4 ± 4.85	<0.05

4 Discussion

The present study explored the concentrations of trace elements, including copper, magnesium, zinc, and iron, in pregnant women with vivax malaria compared to healthy pregnant women. The findings indicated significantly lower levels of these elements in the malaria group. These results align with previous research, suggesting that trace element deficiencies may exacerbate the pathological effects of malaria by compromising immune function and contributing to oxidative stress (14, 21, 22). Trace elements play crucial roles in various biochemical pathways. For example, copper and zinc are essential for antioxidant defense mechanisms and immune function, while iron is critical for oxygen transport and cellular metabolism (13, 14).

In this study, copper deficiency was observed in pregnant women with vivax malaria, corroborating earlier reports that suggested copper's role in reducing oxidative damage through its involvement in scavenging free radicals (20, 21). Zinc deficiency was also noted, supporting the hypothesis that inadequate zinc levels could impair immune response, potentially leading to increased malaria parasitemia (14, 22).

This deficiency has been associated with adverse pregnancy outcomes, such as low birth weight and preterm delivery, due to its essential function in cellular growth and differentiation (23).

The study's strength lies in its focus on vivax malaria, which is often under-researched compared to Plasmodium falciparum. By examining a well-defined cohort of pregnant women in a malaria-endemic region, the research provides valuable insights into the nutritional deficiencies that may worsen the disease's impact. However, the study's limitations should be acknowledged. The relatively small sample size may restrict the generalizability of the findings to larger populations. Additionally, the cross-sectional design limits the ability to establish causality between trace element levels and malaria severity. Other confounding factors, such as dietary habits, socioeconomic status, and genetic predispositions, were not controlled, potentially influencing the trace element concentrations observed.

Future research should focus on larger, longitudinal studies to better understand the causal relationships between trace element deficiencies and malaria outcomes in pregnancy. It is also recommended that interventions, such as nutritional supplementation, be explored to determine their effectiveness in improving pregnancy outcomes and reducing malaria severity. Addressing these nutritional deficiencies could be an essential component of comprehensive malaria management strategies for pregnant women, potentially reducing the incidence of adverse outcomes such as low birth weight and infant mortality (9, 10).

The study highlights the need for healthcare providers to consider nutritional assessments and interventions as part of prenatal care in malaria-endemic regions. By integrating micronutrient supplementation into existing malaria control programs, it may be possible to enhance maternal and fetal health outcomes. This approach should be tailored to the specific nutritional needs of the population and take into account other health determinants to ensure its effectiveness. Overall, the study contributes to a growing body of evidence underscoring the importance of trace elements in modulating immune responses and disease progression in malaria-infected pregnant women (15, 23).

5 Conclusion

In conclusion, this study demonstrated that pregnant women with vivax malaria exhibited significantly lower levels of essential trace elements such as copper, magnesium, zinc, and iron compared to healthy pregnant women. These deficiencies may contribute to the increased susceptibility to malaria and its adverse pregnancy outcomes, including low birth weight and increased infant mortality. Addressing these nutritional deficiencies through targeted supplementation could enhance maternal immunity and improve pregnancy outcomes in malaria-endemic regions. For healthcare providers, incorporating nutritional assessments and tailored supplementation strategies into prenatal care programs could be crucial in mitigating the impact of malaria during pregnancy and improving maternal and child health outcomes.

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Disclaimers

Author Contributions	Saira Baloch and Saira Dars conceptualized and designed the study. Ayesha Farhat contributed to data collection and analysis. Warisha Durani and Ramsha Zafar Durani assisted with laboratory analyses and data interpretation.
Conflict of Interest	The authors declare that there are no conflicts of interest.
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Trial Registration	NA
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