



## Antioxidant vitamins and electrolytes in symptomatic premenopausal women

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### Abstract

**Background:** Menopause signifies the cessation of menstruation, with the premenopausal phase (typically between ages 40 and 45) characterized by hormonal fluctuations, including a decline in estrogen levels and an increase in follicle-stimulating hormone (FSH). This period is associated with various symptoms such as hot flushes, depression, and sleep disturbances. Additionally, deficiencies in vitamins and trace elements during this phase influence oxidative stress and electrolyte balance.

**Objective:** To evaluate the levels and clinical significance of antioxidant vitamins (Vitamin C and Vitamin E) and electrolytes (Sodium and Potassium) in premenopausal women.

**Methods:** The study included 200 participants divided into two groups: 100 women with premenopausal symptoms (Group 1) and 100 age-matched women without symptoms (Group 2).

**Results:** The findings revealed a significant increase in serum sodium levels in premenopausal women, while potassium levels remained unchanged. Levels of antioxidant vitamins, specifically Vitamin C and Vitamin E, were significantly reduced ( $p < 0.0001$ ) in the symptomatic group compared to controls.

**Conclusion:** The decline in estrogen during the premenopausal phase is associated with reduced levels of antioxidant vitamins and elevated serum sodium levels. These changes contribute to the manifestation of premenopausal symptoms, ultimately affecting the quality of life. The assessment of these parameters may facilitate early diagnosis and management of premenopausal symptoms.

**Keywords:** Perimenopause, premenopause, premenopausal symptoms, antioxidant, vitamin c, vitamin e, serum sodium, serum potassium

### Introduction

Menopause is defined as the permanent cessation of menstruation, marking the conclusion of a woman's reproductive life and resulting from the loss of ovarian follicular activity. It is identified as the point at which the final menstrual period occurs. [1] Premenopause refers to the phase preceding menopause, typically encompassing women aged 40–45 years. [2] During this phase, resistance to pituitary gonadotropins triggers a series of physiological changes, including a decline in serum estradiol levels and reduced inhibin production, leading to elevated follicle-stimulating hormone (FSH) levels. [3] These hormonal disturbances make women more vulnerable to physiological, psychological, and sociological changes during the premenopausal period. Furthermore, deficiencies in vitamins and various trace elements are common during this stage. [1, 4]

The menopausal transition, characterized by a decline in estrogen levels, is often accompanied by a range of symptoms. [5] These include hot flushes, nocturnal sweating, sleep disturbances, depression, anxiety, impaired memory and concentration, weight gain, dyslipidemia, vaginal dryness, lower urinary tract infections, dyspareunia, and hair loss, all of which adversely impact quality of life and long-term health. [6]

A significant reduction in estrogen levels during the premenopausal and menopausal phases leads to increased oxidative stress. While physiologically higher estrogen concentrations have a protective effect against oxidative stress, the reduced levels in the perimenopausal state

exacerbate oxidative stress. [7] Estrogen also plays a critical role in maintaining sodium and water balance in the body. [8] In the premenopausal phase, declining estrogen levels result in elevated serum sodium levels, making women more prone to postmenopausal hypertension. [9] The decline in estrogen further disrupts the balance between serum sodium and potassium levels. [10] Against this background, this study aims to assess antioxidant vitamins, specifically Vitamin C and Vitamin E, as well as serum electrolytes (Sodium and Potassium) in women experiencing premenopausal symptoms.

### Materials and methods

This case-control study was conducted at the Raichur Institute of Medical Sciences and Research Centre, Raichur, following approval from the institution's scientific and ethical committee. The study included two groups: women presenting to the Medicine Outpatient Department (OPD) or the Obstetrics and Gynaecology (OBG) OPD with premenopausal symptoms (PMS) were designated as cases, and age-matched women without symptoms served as controls. A total of 100 women with PMS symptoms (Group 1) and 100 asymptomatic age-matched women (Group 2) participated in the study, conducted between August 2023 and January 2024.

Women aged 40–45 presenting to the OBG OPD with a history of irregular periods, vaginal issues, or bladder problems were included as cases, as were women in the same age group visiting the Medicine OPD with complaints such as sleep disturbances, hot flushes, depression, or

feelings of insecurity. Controls consisted of age-matched women attending the OBG and Medicine OPDs for routine health checkups, provided they did not exhibit any PMS symptoms. Women who had undergone hysterectomy or oophorectomy or had not attained menarche were excluded from the study.

Permission was obtained from the respective departments, and all participants were informed about the study in detail, including an explanation in their local language. Participants were clearly informed about the need for a blood sample, and samples were collected only after obtaining their informed consent. All investigations were carried out in the central laboratory of the institute.

For sample collection, 3 mL of venous blood was drawn and allowed to clot at room temperature for one hour. The samples were then centrifuged at 3000 rpm for five minutes to separate the serum. Serum electrolytes were analyzed using the ST-200 electrolyte analyzer with the Ion Selective Electrode (ISE) method, while Vitamin C and Vitamin E levels were measured using the electrochemiluminescence immunoassay (ECLIA) method.

**Statistical analysis:** Statistical analysis was performed using SPSS software version 21.0. Descriptive data were expressed as mean ± standard deviation (SD) and range values. The unpaired Student's t-test was used to compare data between the case and control groups, with a p-value of less than 0.05 considered statistically significant.

**Results**

In the present study, 200 subjects were included and divided into two groups: cases and controls. The control group consisted of 100 healthy women, while the case group comprised 100 women experiencing premenopausal symptoms. The mean age of participants in the case and control groups was 43.42 ± 2.257 and 43.43 ± 2.315 years, respectively, indicating that the groups were age-matched with no statistically significant difference between them.

Serum levels of antioxidant vitamins (Vitamin C and Vitamin E) and electrolytes (Sodium and Potassium) were measured, revealing statistically significant differences between the two groups. Vitamin C levels ranged from 0.5 to 0.7 mg/dL in the case group, with a mean ± standard deviation (SD) of 0.589 ± 0.077 mg/dL. In contrast, the control group had levels ranging from 0.7 to 1.2 mg/dL, with a mean ± SD of 0.976 ± 0.145 mg/dL. This difference was highly statistically significant. Similarly, Vitamin E levels were lower in the case group, ranging from 0.3 to 0.5 mg/dL with a mean ± SD of 0.414 ± 0.073 mg/dL,

compared to the control group, which ranged from 0.5 to 1.0 mg/dL with a mean ± SD of 0.795 ± 0.181 mg/dL. The mean serum sodium concentration was significantly higher in the case group (146.99 ± 4.301 mmol/L) compared to the control group (139.74 ± 2.873 mmol/L). However, no significant difference was observed in serum potassium levels between the two groups.

**Discussion**

In a woman's reproductive life, perimenopause, or the menopausal transition, is a period marked by significant reproductive and hormonal changes. Perimenopause is divided into two phases. [11] The early perimenopause phase, also referred to as the premenopausal phase, is characterized by prolonged amenorrhea lasting more than 60 days. [12] In the late perimenopause phase, declining circulating estrogen levels lead to the cessation of menstruation. [13] The decrease in estrogen levels during this period results in inflammation within the neurological system, which was previously regulated by estrogen. [14] This decline contributes to the onset of premenopausal symptoms, as previously discussed. Symptoms such as fatigue adversely impact women's ability to perform daily tasks, leading to reduced workplace productivity and difficulty concentrating. Additionally, the reduced estrogen levels during the premenopausal phase are associated with increased oxidative stress, which triggers the production of inflammatory cytokines. [15-18]

Antioxidant vitamin levels, including Vitamin C and Vitamin E, decline during the perimenopausal stage. [19] In this study, women with premenopausal symptoms demonstrated significantly reduced levels of these essential vitamins, which are critical for controlling oxidative stress. Serum sodium levels are typically inversely proportional to estrogen levels. In this study, women in the premenopausal phase exhibited elevated serum sodium levels, while potassium levels remained unchanged. [20] These alterations are linked to menopausal hypertension. Administering low doses of estrogen during the menopausal transition (premenopause phase) may help restore sodium and water balance, mitigating these effects. [21]

The present study is not without limitations. Other antioxidant vitamins, such as beta-carotene, as well as commonly studied antioxidants like uric acid and albumin, could also be measured to provide a more comprehensive understanding of oxidative stress in premenopausal women. Additionally, working women were excluded from the study to focus on a more homogenous group and minimize confounding factors related to occupational stress and lifestyle differences.

**Table 1:** Comparison of age and antioxidant vitamins between cases and controls

	Cases Mean ± SD	Controls Mean ± SD	p-value
Age	43.42 ± 2.257	43.43 ± 2.315	0.975
Vitamin C	0.589 ± 0.077	0.976 ± 0.145	<0.001*
Vitamin E	0.414 ± 0.073	0.795 ± 0.181	<0.001*

\*Statistically significant at p<0.05

**Table 2:** Comparison of sodium and potassium between cases and controls

	Cases Mean ± SD	Controls Mean ± SD	p-value
Sodium	146.99 ± 4.301	139.74 ± 2.873	<0.001*
Potassium	4.067 ± 0.422	4.067 ± 0.422	0.914

\*Statistically significant at p<0.05

## Conclusion

Since antioxidant vitamin levels are reduced during the premenopausal phase, oral supplementation of Vitamin C and Vitamin E is recommended. For women who are unable to undergo Hormone Replacement Therapy (HRT), dietary advice can include the consumption of Vitamin C-rich foods such as amla and citrus fruits, as well as Vitamin E-rich foods such as fish liver oil and almonds. These dietary interventions can help alleviate premenopausal symptoms caused by oxidative stress. Incorporating readily available Vitamin C- and Vitamin E-rich foods into the diet can significantly reduce the severity and risk of premenopausal symptoms. For elevated sodium levels, a low-dose estrogen regimen may be considered to help maintain water balance. Additionally, a salt-restricted diet can be recommended to manage sodium levels effectively.

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