



# Selenium Levels based on Various Menopause Complaints Assessed by Menopause-specific Quality of Life Questionnaire before and after Selenium Intervention

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## Abstract

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**BACKGROUND:** Menopausal symptoms can greatly affect a woman's personal, social, and work life. Selenium functions as a cofactor for glutathione peroxidase and helps minimize oxidative damage through cellular metabolism in postmenopausal women when estradiol production decreases, antioxidant protection is lost and therefore oxidative stress is increased.

**AIM:** The aim of the study was to evaluate effect of selenium supplementation on selenium levels based on menopausal complaints assessed by menopause-specific quality of life questionnaire (MENQOL).

**MATERIALS AND METHODS:** This research is an analytical study with quasi-experimental pre-test and post-test one group only design. The research was conducted on all postmenopausal women in Medan who were aged >51-years-old and met inclusion and exclusion criteria. The research subjects underwent blood tests to assess serum selenium levels. If data were normally distributed, dependent T test will be used, while if data were not normally distributed, Wilcoxon test will be used. The analysis results were stated to be significant with  $p < 0.05$ .

**RESULTS:** Mean selenium serum levels before selenium administration were  $93.20 \pm 17.253 \mu\text{g/L}$  which increased to  $132.12 \pm 19.866 \mu\text{g/L}$  after selenium administration. Comparison test results of selenium levels before and after administration found  $p = 0.000$  ( $p < 0.05$ ), which means there was a significant difference of selenium serum levels before and after selenium administration. Besides that, there were no significant scores difference in aspects of vasomotor disorders ( $p = 1.000$  [ $p > 0.05$ ]), psychosocial disorders ( $p = 0.090$  [ $p > 0.05$ ]), physical disorders ( $p = 0.323$  [ $p > 0.05$ ]), and sexual disorders ( $p = 0.959$  [ $p > 0.05$ ]) between before and after selenium administration.

**CONCLUSION:** Total MENQOL scores and complaints based on aspects of vasomotor, psychosocial, physical, and sexual disturbances did not show statistically significant changes after administration selenium tablets 100 mcg/day for 7 days.

## Introduction

Based on the WHO reported, in 2007, there were 55% women aged over 60 years worldwide and increased to 58% women aged over 70 years. In 2007, there were 270 million women aged over 60 living in poor and developing countries. By 2050, it is estimated that 84% of population over were aged over 60 will live in poor and developing countries [1].

Menopause is menstruation cessation that reflects ovulation cessation due to loss of ovarian follicles, which results in decreased ovarian production of estradiol, most biologically active form of estrogen, as well as increased circulating concentrations of follicle stimulating hormone (FSH) and decreased concentrations of inhibin, which inhibits FSH release [2].

Antioxidant status and lipid metabolism both worsen with decreased estrogen levels which amplify risk of oxidative stress-related diseases in menopause. The capacity of estrogens to prevent free radical

scavenging, neutralize effects of increased reactive oxygen species (ROS) and production of antioxidant molecules decreases at menopause [3].

Selenium in the form of selenoprotein functions as an antioxidant to protect ROS and reactive nitrogen species. Selenium functions as cofactor for glutathione peroxidase and helps minimize oxidative damage through cellular metabolism [4]. Selenium deficiency can lead to increased ROS levels, whereas plasma selenium is positively related to bone mineral density in healthy and euthyroid postmenopausal women [5]. Selenium affects thyroid gland function. Changes in thyroid function can result in mood worsening, as well as impaired behavior and cognitive function [6].

Menopause-specific quality of life questionnaire (MENQOL) addresses occurrence and extent of distressing physical and psychological problems that affects women during menopausal transition [7]. MENQOL questionnaire can be used as a tool to predict occurrence of various disorders in menopausal women both physical and psychological aspects [8].

According to Wimmer *et al.*, normal levels of selenium serum were 120–160 µg/l [9]. According to Jenary I. research, mean selenium levels in 35 samples of postmenopausal women in Medan on 2021 was 107.69 µg/L. Regarding correlation between selenium levels and menopausal complaints, it was found that there was a negative correlation between selenium levels and vasomotor disorders aspects ( $p > 0.05$ ), a negative correlation between selenium levels and psychosocial disorders aspects ( $p > 0.05$ ). In this study, there was a weak negative correlation between selenium levels and physical disorders aspects with a correlation coefficient of (-0.386), there was no significant correlation between selenium levels and sexual disorders aspects ( $p > 0.05$ ), and weak negative correlation between selenium levels and MENQOL total score (-0.375) [10].

Examination of selenium levels is cheaper and easier than examination of glutathione peroxidase for early detection of menopausal complaints and selenium supplementation has potential as an additional nutrient in postmenopausal women to maintain menopausal women quality of life. Based on above background, researcher is interested to prove effect of selenium supplementation on selenium levels based on menopausal complaints assessed by MENQOL.

## Materials and Methods

This research is an analytical study with quasi-experimental pre-test and post-test one group only design which was carried out at Prodia S. Parman Clinical Laboratory, Medan in May 2022 until sample was met. The research sample was menopausal women in Medan who were aged >51 years old who met inclusion and exclusion criteria and had signed consent form. To facilitate the analysis, a minimum of 25 patients will be recruited.

The inclusion criteria were willing to participate in this research and take blood samples, fill out questionnaires, and have filled out an informed consent form. In addition, exclusion criteria in this research were: Patients had undergone surgical removal of uterus or ovaries, chemotherapy, radiotherapy in pelvic area, receiving hormone replacement treatment, patients with malignancy (thyroid and breast), and chronic and uncontrolled metabolic diseases (diabetes mellitus and hypertension).

The collected blood samples then examined for selenium levels. This examination was carried out before and after administration of selenium supplementation. Selenium tablets at dose of 100 mcg/day were given to research subjects for 1 week. To analyze differences of selenium levels, an inferential analysis will be carried out. Normality test will be done by Saphiro–Wilk test.

If data were normally distributed, dependent T test will be used, while if data were not normally distributed, Wilcoxon test will be used. The analysis results were stated to be significant with  $p < 0.05$ .

**Table 1: Research subject characteristics data**

Characteristics	n (%)
Age (year old)	
51–60	19 (76)
>60	6 (24)
Education	
Low (Elementary school-junior high school)	14 (56)
Middle (Senior high school)	9 (36)
High (University)	2 (8)
BMI	
Underweight	0
Normal	9 (36)
Overweight	14 (56)
Obese	2 (8)
Menopause duration (years)	
<2	2 (8)
2–5	10 (40)
>5	13 (52)

BMI: Body mass index.

## Results

In this research, research subjects were menopausal women in Medan who were aged more than or equal to 51 years who met the inclusion criteria as many as 25 people. Research subjects characteristics were presented in Table 1.

Based on Table 2, the respondents response results about menopausal symptoms as measured by MENQOL with score of 1 stated as no complaints and score of 2–8 stated as with complaints. The indicator vasomotor disorders aspect found that most complained was easy sweating (40%) which this indicator decreased compared to pre-treatment (44%). Results of comparison test showed that all indicators on vasomotor aspect did not differ significantly between before and after selenium administration ( $p > 0.05$ ). The indicator of psychosocial disorders aspects found that experiencing memory loss is most complained before pretreatment (60%) but increased to 68% in post-treatment. The comparison test results showed that all indicators on psychosocial aspects were not significantly different between before and after selenium administration ( $p > 0.05$ ).

The comparison test results showed that all indicators on physical aspect did not differ significantly between before and after selenium administration ( $p > 0.05$ ), except for muscle and joint pain which had a significant difference between before and after selenium administration ( $p < 0.05$ ). On sexual disorders aspect, most complained after treatment was sexual desire decrease (36%) which decreased compared to pretreatment (48%). The comparison test results showed that all indicators on sexual aspect did not differ significantly between before and after selenium administration ( $p > 0.05$ ).

Selenium levels and menopausal complaints based on MENQOL were compared based on mean

**Table 2: Comparison of symptoms frequency based on level of Menopause-Specific Quality of Life Questionnaire complaints before and after selenium administration**

Symptoms degree	Pre-treatment		Post-treatment		p*
	Complain (-), n (%)	Complain (+), n (%)	Complain (-), n (%)	Complain (+), n (%)	
<b>Vasomotor</b>					
1. Hot flushes on face and neck	20 (80)	5 (20)	21 (84)	4 (16)	1.000
2. Night sweats	17 (68)	8 (32)	18 (72)	7 (28)	0.758
3. Sweating	14 (56)	11 (44)	15 (60)	10 (40)	0.774
<b>Psychosocial</b>					
4. Being dissatisfied with my personal life	21 (84)	4 (16)	21 (84)	4 (16)	1.000
5. Feeling anxious and nervous	18 (72)	7 (28)	15 (60)	10 (40)	0.370
6. Experiencing poor memory	10 (40)	15 (60)	8 (32)	17 (68)	0.556
7. Accomplishing less than I used to	14 (56)	11 (44)	14 (56)	11 (44)	1.000
8. Feeling depressed, down or blue	17 (68)	8 (32)	12 (48)	13 (52)	0.152
9. Being impatient with other people	15 (60)	10 (40)	13 (52)	12 (48)	0.569
10. Feeling of wanting to be alone	21 (84)	4 (16)	19 (76)	6 (24)	0.480
<b>Physicals</b>					
11. Flatulence (wind) or gas pains	9 (36)	16 (64)	11 (44)	14 (56)	0.564
12. Aching in muscles and joints	1 (4)	24 (96)	8 (32)	17 (68)	0.023
13. Feeling tired or worn out	10 (40)	15 (60)	7 (28)	18 (72)	0.370
14. Difficulty sleeping	13 (52)	12 (48)	15 (60)	10 (40)	0.569
15. Aches in back of neck or head	14 (56)	11 (44)	10 (40)	15 (60)	0.258
16. Decrease in physical strength	8 (32)	17 (68)	7 (28)	18 (72)	0.758
17. Decrease in stamina	4 (16)	21 (84)	10 (40)	15 (60)	0.059
18. Feeling a lack of energy	4 (16)	21 (84)	8 (32)	17 (68)	0.185
19. Drying skin	8 (32)	17 (68)	13 (52)	12 (48)	0.152
20. Weight gain	17 (68)	8 (32)	17 (68)	8 (32)	1.000
21. Increased facial hair	20 (80)	5 (20)	22 (88)	3 (12)	0.702
22. Changes in appearance, texture or tone of your skin	12 (48)	13 (52)	16 (64)	9 (36)	0.254
23. Feeling bloated	23 (92)	2 (8)	21 (84)	4 (16)	0.667
24. Low Backache	14 (56)	11 (44)	12 (48)	13 (52)	0.571
25. Frequent urination	11 (44)	14 (56)	11 (44)	14 (56)	1.000
26. Involuntary urination when laughing or coughing	15 (60)	10 (40)	16 (64)	9 (36)	0.771
<b>Sexual</b>					
27. Change in your sexual desire	13 (52)	12 (48)	16 (64)	9 (36)	0.390
28. Vaginal dryness during intercourse	16 (64)	9 (36)	16 (64)	9 (36)	1.000
29. Avoiding intimacy	15 (60)	10 (40)	16 (64)	9 (36)	0.771

\*Chi-square test.

values before (pre-treatment) and after (post-treatment) selenium administration using mean test of two paired samples.

Based on Table 3, mean serum selenium level before selenium administration was  $93.20 \pm 17.253 \mu\text{g/L}$  which then increased to  $132.12 \pm 19.866 \mu\text{g/L}$  after selenium administration. The comparison test results between before and after administration of selenium obtained  $p = 0.000$  ( $p < 0.05$ ), which means there was a significant difference in serum selenium levels before and after selenium administration described on Table 4. The comparison test results between before and after selenium administration showed that there was no significant scores difference in aspects of vasomotor disorders ( $p = 1.000$  [ $p > 0.05$ ]), psychosocial disorders ( $p = 0.090$  [ $p > 0.05$ ]), physical disorders ( $p = 0.323$  [ $p > 0.05$ ]), and sexual disorders ( $p = 0.959$  [ $p > 0.05$ ]) between before and after selenium administration.

The results based on Table 5 showed a negative correlation between selenium levels and total MENQOL score, aspects of vasomotor disorders, aspects of psychosocial disorders, and aspects of physical disorders before selenium administration. However, correlation between four indicators was not statistically significant ( $p > 0.05$ ). Bivariate test to evaluated correlation between selenium levels and aspects of sexual disorders before selenium administration found positive correlation, but correlation between selenium levels and aspects of sexual disorders before selenium administration was not statistically significant ( $p > 0.05$ ).

The results showed negative correlation between selenium levels and total MENQOL score,

aspects of vasomotor disorders, aspects of psychosocial disorders, and aspects of sexual disorders after selenium administration. However, correlation between four indications was not statistically significant ( $p > 0.05$ ). In correlation test between selenium levels and aspects of physical disorders after selenium administration found positive correlation, but correlation test between selenium levels and aspects of physical disorders after selenium administration was not statistically significant ( $p > 0.05$ ).

## Discussion

Low selenium levels in this research were not associated with menopausal complaints based on MENQOL score. These results are in line with the previous studies that in overweight and obese postmenopausal women, serum selenium levels were not associated with quality of life based on physical, sexual, and menopausal health aspects [11]. However, these results are not in line with Placido *et al.* research which showed decrease in quality of life according to decrease in selenium levels, menopausal symptoms will increase and be severe in postmenopausal women [12]. Basically, selenium in the form of selenocysteine is a catalyst for enzyme glutathione peroxidase in mammals, including humans. Glutathione peroxidase is an antioxidant enzyme that can be used as a marker of menopausal complaints severity [13]. However, in this research, there was no relationship between selenium levels and menopausal complaints.

Llaneza et al. explained that there was no effect of selenium administration on menopausal women's quality of life because menopausal women were obese and overweight. The food consumed tends to be high in saturated fat but low in total fat, fruit, vegetables, and fiber which causes low intake of antioxidants [11].

**Table 3: Comparison of selenium levels and menopausal complaints before and after selenium administration**

Variable	n	Range (minimum–maximum)	Mean ± SD	p
Selenium levels (pre) (µg/L)	25	70,00–141,00	93.20 ± 17.253	0.000 <sup>b</sup>
Selenium levels (post) (µg/L)	25	91,00–179,00	132.12 ± 19.866	
MENQOL total score (pre)	25	35–147	76.20 ± 28.34	0.809 <sup>b</sup>
MENQOL total score (post)	25	41–155	75.12 ± 29.55	
Aspects of vasomotor disorders (pre)	25	3–24	6.64 ± 5.15	1.000 <sup>b</sup>
Aspects of vasomotor disorders (post)	25	3–18	6.16 ± 4.49	
Aspects of psychosocial disorders (pre)	25	7–36	15.32 ± 8.49	0.090 <sup>b</sup>
Aspects of psychosocial disorders (post)	25	7–37	17.08 ± 8.13	
Aspects of physics disorders (pre)	25	22–84	46.80 ± 16.35	0.323 <sup>a</sup>
Aspects of physics disorders (post)	25	23–79	44.36 ± 15.88	
Aspects of sexual disorders (pre)	25	3–20	7.44 ± 4.93	0.959 <sup>b</sup>
Aspects of sexual disorders (post)	25	3–24	7.52–6.00	

\*Paired t-test, \*\*Wilcoxon test, p < 0.05 = Significant. Pre: Before selenium administration, Post: After selenium administration. SD: Standard deviation, MENQOL: Menopause-specific Quality of Life Questionnaire.

In this research results, selenium supplementation was able to increase serum selenium levels to 132.12 ± 19.866 µg/L where normal range of selenium levels was 120–160 g/L. Research by Ha Eun Jeung on healthy American postmenopausal women showed that maintaining selenium levels by consuming foods containing selenium above RDA (average intake of 90 mcg/day) for approximately 1 week was able to increase action of enzyme glutathione peroxidase [14]. The comparison test results between before and after selenium administration obtained p = 0.000 (p < 0.05), which means there was a significant serum selenium levels differences between before and after selenium administration. These results are in line with studies in sheep that supplementation with Selenium 0.15 mg/kg increased serum Se levels linearly with increasing duration of experimental feeding for 30; 60; and 90 days.<sup>21</sup> Similar results were reported that 12 weeks of supplementation with 400 mg Q10 and 200 g selenium per day in women aged 58 years significantly increased serum Q10 and selenium levels compared with placebo [15].

**Table 4: Correlation between selenium levels and menopausal complaints based on Menopause-specific Quality of Life Questionnaire before selenium administration**

Correlation pretreatment	n	R	p
Selenium level-MENQOL total score	25	-0.176	0.400
Selenium levels-aspects of vasomotor disorders	25	-0.180	0.389
Selenium levels-aspects of psychosocial disorders	25	-0.146	0.488
Selenium levels-aspects of physical disorders	25	-0.184	0.378
Selenium levels-aspects of sexual disorders	25	0.039	0.855

Pearson correlation test, p < 0.05 = Significant. MENQOL: Menopause-specific Quality of Life Questionnaire.

In this research, there was no correlation between selenium levels and menopausal complaints based on MENQOL on all disorder aspects both before and after selenium administration. In the previous study, it was reported by Jenary I., that there was a negative correlation between selenium levels and menopausal complaints based on aspects of physical disorders [10]. These results are inconsistent with the previous studies which stated that effects of deteriorating mood, as well as impaired behavior

and cognitive function in menopause can be reduced by selenium supplementation. Selenium increases macrophage activity and immunoglobulin production and also increases cytotoxicity and NK (natural killer) cells. Selenium slows the aging process by increasing tissue flexibility. In addition, it relieves symptoms that occur during menopause [6]. In this research, selenium tablets of 100 mcg/day for 7 days were only able to reduce muscle and joint pain. In Muharram et al. research, physical domain, joint, and muscle pain are most complained of menopause symptoms [16]. Regarding behavioral changes, it is stated that behavior changes can occur in approximately 10 weeks [17].

**Table 5: Correlation between selenium levels and menopausal complaints based on menopause-specific quality of life questionnaire after selenium administration**

Correlation post treatment	n	R	p
Selenium level-MENQOL total score	25	-0.022	0.915
Selenium levels-aspects of vasomotor disorders	25	-0.109	0.604
Selenium levels-aspects of psychosocial disorders	25	-0.055	0.793
Selenium levels-aspects of physical disorders	25	0.032	0.878
Selenium levels-aspects of sexual disorders	25	-0.040	0.849

Pearson correlation test, p < 0.05 = Significant. MENQOL: Menopause-specific Quality of Life Questionnaire.

The research results explain that effect of selenium supplementation on reducing muscle and joint pain can be explained as follows. In the previous studies, it was reported that selenium plays an important role in bone formation and bone metabolism. In addition, Selenium can enhance osteoblastic differentiation of bone marrow mesenchymal stem cells by inhibiting differentiation and formation of mature osteoclasts *in vitro*. Since many metal ions have an osteoinductive effect, the incorporation of various therapeutic ions into biomaterial is an effective strategy for stimulating bone regeneration [18]. Compared to boron, iron, zinc, and copper, selenium is a trace element present in bone that affects bone metabolism. Selenium supplements promote GPx and TrxR activity, and GPx activity is more activated in people with selenium deficiency status. GPx and TrxR suppress NFκB activation at supranutritional selenium levels and regulate osteoclastogenesis and osteoblastogenesis. Cotreatment 1α,25 (OH)2D3 and selenium synergistically increased protein and TrxR1 activity [19].

In this research reported that although selenium supplementation could significantly increase serum selenium levels, there was no significant change in clinical aspects, namely, changes in menopausal complaints. One of reasons is limited strong evidence regarding correlation between selenium levels and menopausal complaints, especially MENQOL scores, and this research results also reported that there was no significant relationship between menopausal levels and menopausal complaints based on MENQOL scores both before and after selenium treatment. Muharam et al. also reported similar results related to absence of a significant change in clinical aspect of MENQOL complaints after supplementation of 120 mg daidzein for 8 weeks [16].

In addition, it was also reported that several disorders in elderly due to low serum selenium levels include cardiovascular disease, poor cognitive function, and reduced muscle strength. However, results relating selenium supplementation in muscle also suggest that supplementation of 200 g/day for 26 weeks did not affect bone turnover (as assessed by NTX/Cr) and did not benefit musculoskeletal health in postmenopausal women [20].

## Conclusion

Total MENQOL scores and complaints based on aspects of vasomotor, psychosocial, physical, and sexual disturbances did not show statistically significant changes after administration selenium tablets 100 mcg/day for 7 days.

## Acknowledgment

Research needs to be done to find other parameters besides selenium which is likely to be closely correlated with menopausal symptoms so that people with menopausal symptoms can later be given adequate food intake more precisely contains these parameters. Further research is needed regarding the correlation of selenium levels with menopausal complaints based on normal and abnormal grouping of selenium levels.

## Ethical Approval

Health Research Ethical Committee, Universitas Sumatera Utara, Medan, Indonesia, approved this study.

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