

## RESEARCH ARTICLE

# Evaluation of association between psychological stress level during menopausal transition period and serum estrogen level among middle-aged women: A cross-sectional study

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### ABSTRACT

**Background:** Menopause is a gradual transition from reproductive to non-reproductive phase in women during which there is substantial fluctuation in estrogen or estrogen deficiency. Furthermore, women encounter various psychological, physical symptoms during this transition period. Timely diagnosis can result in appropriate interventions to reduce these symptoms and result in uneventful transition period. **Aims and Objectives:** To evaluate the association between psychological symptoms during menopausal transition period and serum estrogen levels. **Materials and Methods:** Seventy-five women volunteers in the age group of 45-60 years (perimenopausal (PM) with symptoms, PM without symptoms, PM women - 25 in each group) were evaluated for symptoms of menopausal transition using Women Health Questionnaire. Serum estrogen level was estimated by enzyme-linked immunosorbent assay method. **Results:** The study showed that there was a significant difference in psychological stress levels quantified as stress scores among three groups, with symptomatic PM women having much higher stress levels compared to other groups. Correlation statistics showed that there was a significant correlation between serum estrogen levels and psychological stress level. There was a significant correlation between anxiety depression mood disturbances, vasomotor symptoms, and symptoms of well-being with serum estrogen level. **Conclusions:** The symptoms of menopausal transition are attributed to reduction in estrogen level. These symptoms lead to substantial psychological stress among women during PM transition period.


**KEY WORDS:** Perimenopause; Menopausal Transition Symptoms; Estrogen

### INTRODUCTION

The reproductive period of women, gradually transcends into a stage of perimenopause, followed by menopause after a couple of years.<sup>[1]</sup> Perimenopause is a transitional stage which is before menopause which can range from 2 to 10 years. In this stage, the menstrual periods are irregular, with a 30%

reduction in estrogen and a decrease in progesterone.<sup>[1]</sup> The changes in hormonal status during this period, mainly estrogen has potent and long-lasting influence on vital organ systems.<sup>[2]</sup> In addition to, cardiovascular risk, reduction in estrogen level, also results in climacteric symptoms like vasomotor, psychological or musculoskeletal disturbances that may contribute to stress among women during this period.<sup>[3]</sup> Psychological stress itself is an individual risk factor for cardiovascular disease (CVD).<sup>[4]</sup>

Vasomotor symptoms (VMS) such as hot flushes and night sweats are the main physical signs of menopause that occur in 50-70% of women during menopausal transition period.<sup>[2]</sup> In addition to VMS, women also experience symptoms such

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as anxiety, mood changes, cognitive deficits, and somatic symptoms (SOM). However, perimenopausal (PM) women experience these symptoms comparatively more than PM women.<sup>[5]</sup>

Symptoms of menopausal transition may be attributed to reduction in beneficial effects of estrogen.<sup>[6]</sup> Premenopausal women have a lower risk of CVD. Following menopause, women tend to have increased risk of metabolic syndrome including dyslipidemia, insulin resistance, hypertension, CVD.<sup>[7,8]</sup> Furthermore, persistent VMS are markers of subclinical CVD. Based on this fact, the study aims at evaluating the association of symptoms of menopausal transition period with serum estrogen level among middle-aged women.

## MATERIALS AND METHODS

This is a cross-sectional study conducted among 75 women volunteers (postmenopausal women, perimenopausal women with and without symptoms [PMS and PMNS] = 25 in each group) in the age group of 45-60 years. Volunteers were recruited from the staff community after explaining the procedure in detail and obtaining a written informed consent. The study was approved by the Institutional Ethics Committee. PMS and PMNS women and postmenopausal women (both surgical and natural menopause) were included in the study. Those participants with a history of diabetes mellitus, hypertension, or any other chronic medical illness, women on hormone replacement therapy were excluded from the study. The menopausal status was classified according to the Stages of Reproductive Aging Workshop<sup>[9,10]</sup> classification which divided menopause staging into: (a) Postmenopausal, (b) late perimenopause, and (c) early perimenopause. Anthropometric measurement such as height and weight was measured. Height was measured to the nearest 0.01 m using stadiometer. Weight was measured to a nearest 0.1 kg using electronic weighing machine. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Assessment of menopause-associated symptoms was performed using the Women's Health Questionnaire (WHQ).<sup>[11,12]</sup> The WHQ is a 23 - item self-reported health-related quality of life scale that was designed to assess a wide range of physical and emotional symptoms, or sensations, experienced by middle-aged women. There were four response options for each item, ranging from 1 to 4, where 1 means "yes definitely" and 4 means "no, not at all." This provides scores on six factors: Anxiety and depressed mood, well-being (WLB), SOM, memory and concentration, VMS, and sleep problems. Two optional factors are available: Sexual dysfunction and menstrual symptoms. Raw scores can be calculated for each scale. Transformed scores can be obtained from raw scores. Scores vary from 0, which indicates a "poor health status" (women experiences symptoms) to 100 (not symptomatic), which indicates a "good health status." Venous blood

samples were collected from all the participants using sterile techniques. Samples were centrifuged and serum estrogen was estimated using enzyme-linked immunosorbent assay (ELISA) method (Total Oestrogen ELISA Kit, Calbiotech, USA).

## Statistical Analysis

Continuous data were expressed as mean  $\pm$  standard error. Intergroup comparison of parameters of psychological stress scores, serum estrogen levels between three groups (PMS, PMNS, and PM women) was done by one way ANOVA with *post hoc* test. If data are not normally distributed Kruskal Wallis test was used. Pearson's correlation test was used for correlation between symptoms of menopause transition and serum estrogen levels.  $P \leq 0.05$  was considered as statistically significant.

## RESULTS

Table 1 shows demographic characteristics of participants among the 3 study groups. The PM women were of higher age group when compared to PMNS and PMS women with  $P = 0.001$  and  $P = 0.006$ , respectively. There was no significant difference in height, weight, and BMI among three groups. Systolic blood pressure (SBP) was higher among postmenopausal women, and it was significant when compared with PMNS and PMS women ( $P = 0.001$  and  $P = 0.008$ , respectively). Heart rate was not significantly different between three study groups.

Table 2 shows parameters of psychological stress level expressed as stress scores among PMNS, PMS, and PM women. There was a significant difference in symptoms of menopausal transition such as anxiety depression mood (ADM), VMS, WLB, memory disturbances, sleep disturbances (SLP), and SOM among PMNS and PMS women. Furthermore, there was a significant difference in

**Table 1:** Participants characteristics, anthropometric parameters, and blood pressure parameters among the three study groups ( $n=75$ )

Variables	PMNS	PMS	PM
Age (years)	46 $\pm$ 3*	46 $\pm$ 3*	51 $\pm$ 4
Weight (kg)	59.51 $\pm$ 1.90	58.39 $\pm$ 1.96	56.84 $\pm$ 1.93
Height (m)	1.55 $\pm$ 0.12	1.55 $\pm$ 0.12	1.55 $\pm$ 0.02
BMI (kg/m <sup>2</sup> )	24.76 $\pm$ 0.60	24.24 $\pm$ 0.57	23.68 $\pm$ 0.60
SBP (mmHg)	115.79 $\pm$ 15.90*	119.33 $\pm$ 19.94*	133.63 $\pm$ 5.78
DBP (mmHg)	75.90 $\pm$ 13.45	78 $\pm$ 12.40	95 $\pm$ 12.39
Basal heart rate	73.74 $\pm$ 7.94	72.80 $\pm$ 8.20	71.83 $\pm$ 7.56

\*Significantly different from PM women, statistical significance at  $P < 0.01$ , data expressed as mean $\pm$ SD. PMNS: Perimenopausal without symptoms, PMS: Perimenopausal with symptoms, PM: Postmenopausal, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation

symptoms of menopausal transition among PMS women and PM women.

Table 3 shows serum estrogen level among PMNS, PMS, and PM women. There was a significant association between serum estrogen levels among PMS and PMNS women with  $P = 0.01$ , those with symptoms having lesser serum estrogen levels than those without symptoms.

**Table 2: Parameters of psychological stress level among PMNS, PMS, and PM women (n=75)**

Variables	PMNS	PMS	PM
ADM	93.33±2.62*	43.33±3.89**	89.09±3.38
VSM	96.67±1.95*	52.5±7.58**	86.11±5.82
WLB	97.08±1.25*	64.67±3.63**	95.83±2.24
MEM	86.67±3.28*	55.56±3.95**	85.19±3.82
SLE	88.33±4.20*	34.17±5.86**	86.11±5.08
SOM	84±4.03*	41±3.36**	83.89±4.56

\*Varies significantly from perimenopausal with symptoms, \*\*varies significantly from postmenopausal women, # $P < 0.05$  considered to be statistically significant,  $p < 0.001$  for all the symptoms between PMNS and PMS, also,  $p < 0.001$  for all the symptoms between PMS and PM. PMNS: Perimenopausal without symptoms, PMS: Perimenopausal with symptoms, PM: Postmenopausal, MSCL: Mean skin conductance level, ADM: Anxiety depression mood, VSM: Vasomotor symptoms, WLB: Well-being, MEM: Memory disturbances, SLP: Sleep disturbances, SOM: Somatic symptoms

**Table 3: Serum estrogen level among PMNS, PMS and PM women (n=75)**

Variables	PMNS	PMS	PM
Estrogen level	90.98±7.34*#	59.07±7.38	37.88±5.77

Data expressed as mean±SE, \*varies significantly from perimenopausal with symptoms and postmenopausal women, # $P < 0.05$  considered to be statistically significant. PMNS: Perimenopausal without symptoms, PMS: Perimenopausal with symptoms, PM: Postmenopausal, SE: Standard error

**Table 4: Correlation between symptoms of menopausal transition (psychological stress scores) and serum estrogen level**

Variables	Serum estrogen level	
	r value	P value
ADM	0.3	0.02*
VSM	0.1	0.03*
WLB	0.31	0.01*
MEM	0.06	0.6
SLE	0.21	0.09
SOM	0.15	0.2

\* $P < 0.05$  considered to be statistically significant. ADM: Anxiety depression mood, VSM: Vasomotor symptoms, WLB: Well-being, MEM: Memory disturbances, SLP: Sleep disturbances, SOM: Somatic symptoms

Table 4 shows correlation between symptoms of menopausal transition and serum estrogen level. There was a significant correlation between scores of ADM, VMS, and symptoms of WLB with serum estrogen level. However, other symptoms of menopausal transition had no significant correlation with serum estrogen level.

## DISCUSSION

The study assesses psychological stress level among middle-aged women and its association with serum estrogen level. During the transition period from perimenopause to menopause, myriad of vague symptoms centered around, vasomotor, and emotional disturbances tend to detract the health status of women. Often, clinical diagnosis of menopause is based on subjective perception of climacteric symptoms during menopausal transition period. There is no consensus and little evidence-based data are available regarding treatment of PMS. The timely assessment of these symptoms during perimenopausal period can decrease the psychological burden that women encounter during this transition period. Moreover, most of the studies' focus on study of these symptoms following menopause, very few studies have given importance to PM transition symptoms among middle-aged women.

In the present study, the SBP was significantly higher among postmenopausal women when compared to PM women. A cross-sectional study that focused on the relative influence of menopausal status on blood pressure levels of healthy women aged 35-60 years showed that both SBP and diastolic blood pressure (DBP) changed with menopausal status. However, the same study also concluded that DBP was higher only among women who attained surgical menopause, which was attributed to abrupt withdrawal of ovarian function that would lead to hormonal imbalance.<sup>[13]</sup> In the present study, there was no significant difference in DBP. Estrogen is known to have direct protective effects on the arterial wall such as vasodilation, inhibition of smooth cell proliferation, thereby modulating response to injury and deprivation of estrogen seems to increase the prevalence of hypertension among postmenopausal women.<sup>[14]</sup> The present study also shows a considerable decrease in estrogen levels among postmenopausal women. However, mean estrogen levels estimated among postmenopausal women was slightly higher than reference range of serum estradiol (7-40 pg/ml) in the present study. This may be due to the fact that duration following menopause among most of the women who participated in the study was within 1-2 years. This is supported by studies by Metcalf et al. which concluded that episodes of significant estrogen production were not uncommon in the 1<sup>st</sup> year after the final menstruation.<sup>[15]</sup>

Furthermore, there was a significant difference in psychological stress scores among three groups, stress scores

being lower in those women with symptoms when compared with other two groups. Similarly, serum estrogen levels were significantly lower among PMS women when compared to women without symptoms and postmenopausal group. Wahdi *et al.*<sup>[16]</sup> showed that estradiol serum levels were lower in women with than those without vasomotor syndromes. However, this study does not explain the difference of estradiol serum levels between the severity of vasomotor symptom.<sup>[17]</sup> During early perimenopause, mid-cycle estrogen concentrations have been observed to be normal or increased. This is owing to the fact that estradiol levels do not gradually decrease; instead, fluctuates greatly around the normal range until menopause, when no more responsive follicles are available. Moreover, the anovulatory cycles may be often associated with elevated levels of estradiol. This may be the reason for significant difference in estrogen levels among PMS and PMNS women in the present study. However, the main cause for PM fluctuations in estradiol is a reduced follicle pool as well as reduced responsiveness of aging ovary to follicle stimulating hormone (FSH). Thus, greater circulating amounts of FSH are needed to initiate folliculogenesis which leads to overstimulation of the ovary causing, relative hyperestrogenemia during this transition period.<sup>[18]</sup> A meta-analysis of various comparative studies, which included premenopausal women and PM women, showed that follicular phase estradiol levels were 30% higher among PM women.<sup>[19]</sup> It is also known that the basic cause of symptoms of menopausal transition is complex relationship with estrogen metabolism and autonomic nervous system. This is confirmed by a study by Lee *et al.* that showed an increase in sympathetic activity among PMS women.<sup>[20]</sup> Increased sympathetic activity may be a link between reduction in estrogen and psychological stress during menopausal transition period.

Findings of the present study showed that there was a significant association between symptoms of menopausal transition mainly, ADM disturbances, VMS and symptoms of WLB with serum estrogen levels. However, VMS (hot flushes and night sweats) are common also in postmenopausal women. Hot flushes and night sweats in menopausal women are attributed mainly to estrogen “deficiency.” This is proved by fact that menopausal women who were being treated with estradiol implants every 6 months had severe hot flushes, irritability, and SLP at a time when their estradiol levels were higher than mid-cycle estrogen peak levels.<sup>[21]</sup> This suggests that VMS arise because the hypothalamus has become used to higher estrogen levels and hot flushes develop when estrogen levels decrease from high to normal as from normal to low. Estrogen withdrawal from previously higher levels likely explains why night sweats and hot flushes occur in 37% of PM women. Mood disorders are likely result of estradiol, which amplifies the stress hormone responses to life stresses.<sup>[22]</sup>

## CONCLUSIONS

The study concludes that the symptoms of menopausal transition are attributed to reduction in estrogen level. These symptoms lead to substantial psychological stress among women during PM transition period.

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