# Assessment of Menopausal Symptoms During Perimenopause and Postmenopause in Tertiary Care Hospital

Marya Ahsan, Ayaz Khurram Mallick<sup>1</sup>, Rashmi Singh, Raj Ranjan Prasad<sup>2</sup>

Departments of Pharmacology and <sup>1</sup>Biochemistry, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, <sup>2</sup>Department of Pharmacology, Nalanda Medical College and Hospital, Patna, Bihar, India

# ABSTRACT

**Background:** Issues related to menopausal symptoms are very complicated in terms of experience, severity, and dynamics of the symptoms. Studies have shown that these symptoms vary among individuals depending on the menopausal stage, ethnicity, geographical location, and other factors. Menopause Rating Scale (MRS) is an effective tool to assess the severity of these symptoms. **Aim:** This study was done to compare the frequency and severity of menopausal symptoms during peri- and postmenopause using the MRS. **Subjects and Methods:** Ninety-two perimenopausal women and 95 postmenopausal women who attended Gynecology out patient department (OPD) for treatment of menopausal complaints were assessed using the MRS questionnaire before starting therapy. Informed consent and ethics committee clearance was obtained prior to the study. Response was recorded and statistical analysis was done using Statistical Package for Social Sciences (SPSS) software version 17.0 (SPSS Inc, Chicago, IL, USA). **Result:** The mean total MRS score was comparable in both the groups. The mean psychological score was significantly higher in perimenopausal group in comparison to postmenopausal group (P < 0.01). The mean urogenital score was higher in postmenopausal women (P < 0.001). **Conclusion:** Fatigue, depression, anxiety, hot flashes, and sexual disturbances were the common symptoms that appeared first during the perimenopausal phase. As the age advanced and women progressed in the postmenopausal stage, the psychological symptoms of depression, irritability, and sleep disturbances decreased; while the urogenital symptoms, fatigue, and generalized body ache became more prominent.

KEY WORDS: Africa, menopause, menopause rating scale, perimenopause, postmenopause, severity of menopausal symptoms

#### INTRODUCTION

Menopause is a significant stage marking the end of a woman's reproductive life. Although this process is physiological, it is plagued by wide range of discomforting features which affects their quality of life. These symptoms includes years of hot flashes associated with episodes of sweating; sleep disturbances; joint pains; and urogenital symptoms such as decrease in libido, dyspareunia, and bladder incontinence. <sup>[1-3]</sup> These symptoms are primarily due to alteration in the hormonal levels, particularly estrogen; which in turn is caused by aging of the ovaries. <sup>[4-6]</sup>

Studies have shown that the frequency of these symptoms and their stability varies. Some occur frequently during

| Access this article online |                                  |  |  |  |
|----------------------------|----------------------------------|--|--|--|
| Quick Response Code        | Website: www.jbcrs.org  DOI: *** |  |  |  |

perimenopause, while others increase progressively from peri- to postmenopause. Hence, the issues related to menopause are very complicated in terms of experience, severity, and dynamics of the symptoms.<sup>[7-10]</sup>

Lower age of menopause in India compared to the West along with increased life expectancy has resulted in a woman today spending almost a third of her life in menopause and that too with distressing clinical problems. [11-15] Common menopausal symptoms among Indian women have been identified, but no study describes these symptoms in terms of both frequency and severity. This is necessary to provide the best therapy to manage these symptoms. This study was aimed to compare the baseline menopausal symptoms of perimenopausal and postmenopausal women seeking treatment for menopausal complains in tertiary care hospital using the Menopause Rating Scale (MRS), which is an internationally accepted tool for this purpose. [16-18]

#### **Address for correspondence**

Dr. Marya Ahsan, Department of Pharmacology, Rohilkhand Medical College and Hospital, Bareilly - 243 006, Uttar Pradesh, India. E-mail: marya\_ahsan@yahoo.co.in

### SUBJECTS AND METHODS

#### Study design

This questionnaire-based study was carried out at a tertiary care hospital in Patna on patients attending Gynecology outpatient department (OPD) for treatment of menopausal complains. The study was approved by the Institutional Ethics Committee and consent was obtained from the patients to participate. The study was carried out from October 2012 to October 2013. A total of 187 patients between 40 and 65 years of age were randomly selected from those who had reported to the OPD with complaints of menopausal symptoms. Of these 92 were perimenopausal and 95 were postmenopausal according to the Stages of Reproductive Aging Workshop (STRAW) +10 criteria.[19] Patients with undiagnosed vaginal bleeding, cardiac disease, liver disorder, diabetes mellitus, breast tumor, or other malignancies; history of stroke or transient ischemic attack; and history of hormonal treatment or soybean derived products in previous 12 months were excluded from the study.

#### Instrument and data collection

The pretested questionnaire consisted of three sections: A, B, and C. Section A consisted of sociodemographic data which included age, marital status, religion, educational, and occupational background. Section B dealt with detailed menstrual history and included assessment of menopausal status of the patient according to the STRAW + 10 classification which divided menopausal staging into: Postmenopausal (no menstrual bleeding in the last 12 months); late perimenopausal (amenorrhea  $\geq$ 60 days); and early perimenopausal (irregular menses without skipping cycles and more than 7 day difference in length of consecutive cycles).<sup>[19]</sup>

The late and early perimenopausal patients were clubbed as the perimenopausal group for ease of statistical analysis.

In section C, the English version of the MRS questionnaire was used as a tool for assessing menopausal symptoms. The MRS questionnaire includes 11 symptoms on a scoring scale from "0" (none) to "4" (very severe symptoms). The symptoms were further grouped into three subscales: somatic, psychological, and urogenital. The English version of MRS which is formally validated scale according to the requirements for quality of life instrument was used in the study. As most of the participants did not know English, the questionnaire was administered by face-to-face interview in the local language by a dedicated postgraduate student. Patients answering mild and moderate were grouped as one and those answering severe to very severe were also grouped together while calculating the prevalence. This was done to eliminate any bias while choosing the best response.

## Statistical analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) software version 17.0 (SPSS Inc, Chicago, IL, USA). Results are presented as number (percentage) and mean  $\pm$  standard deviation wherever appropriate. Chi-square test was applied to compare the frequency and severity of symptoms among the peri- and postmenopausal group. P < 0.05 was considered as the cut-off value for significance.

## **RESULT**

The mean age of the perimenopausal group was 43.45 (2.02) years and that of postmenopausal group was 48.52 (2.27) years. Among the postmenopausal women, the mean age of menopause observed in our study was 45.29 (2.17) years. The frequency and severity of menopausal symptoms experienced by the peri-and postmenopausal women, respectively as assessed by MRS is depicted in Table 1. Most of the women belonged to middle socioeconomic group and had almost similar educational background, hence it did not significantly affect the difference in their responses.

The mean total response score of the perimenopausal group was 21.4 (5.11) and that of the postmenopausal group was 20.01 (3.99) [Figure 1]. The mean score for somatic subscale and psychological scale was higher in perimenopausal women in comparison with postmenopausal women. The increase in psychological subscale was statistically significant (P < 0.01). However, the mean score for urogenital subscale was significantly higher (P < 0.001) in postmenopausal women [Figure 2]. Reliability test of the MRS questionnaire responses yielded Cronbach's alpha of the somatic subscale 0.740, psychological subscale 0.718, and urogenital subscale 0.718. These scores indicate that the response were reliable.

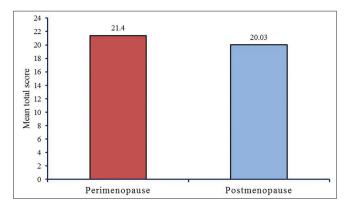
## **DISCUSSION**

Menopause is characterized by an estrogen deficient state and is often met with fear by many women.<sup>[20]</sup> As many organs of the body are sensitive to estrogen, a reduction in estrogen level gives rise to a number of physical, psychological, and sexual changes.<sup>[21]</sup> Studies have shown that the frequency of the symptoms varies over time. Some happen frequently in the perimenopause and decrease over time, while others increase progressively from perimenopause to postmenopause and become more severe towards the end of life.<sup>[7-10]</sup>

Besides the menopausal status, ethnic variations also affect the prevalence and severity of menopausal symptoms.<sup>[22,23]</sup>

Table 1: Frequency and severity of menopausal symptoms among the perimenopausal (n=92) and postmenopausal women (n=95) on the menopause rating scale

| Menopausal symptoms            | Perimenopause (n=92) (%) |                  |                       | Postmenopause (n=95) (%) |                  |                       |
|--------------------------------|--------------------------|------------------|-----------------------|--------------------------|------------------|-----------------------|
|                                | No symptom               | Mild to moderate | Severe to very severe | No symptom               | Mild to moderate | Severe to very severe |
| Somatic                        |                          |                  |                       |                          |                  |                       |
| Hot flashes                    | 31 (33.70)               | 33 (35.87)       | 28 (30.43)            | 44 (46.32)               | 48 (50.53)       | 3 (3.16)              |
| Cardiac symptoms               | 28 (30.43)               | 58 (63.04)       | 6 (6.52)              | 22 (23.16)               | 67 (70.53)       | 6 (6.32)              |
| Sleep disturbances             | 42 (45.65)               | 38 (41.30)       | 12 (13.04)            | 52 (54.74)               | 43 (45.26)       | 0                     |
| Joint and muscle discomfort    | 0                        | 49 (53.26)       | 43 (46.74)            | 0                        | 9 (9.47)         | 86 (90.53)            |
| Psychological                  |                          |                  |                       |                          |                  |                       |
| Depression                     | 6 (6.52)                 | 71 (77.17)       | 15 (16.30)            | 58 (61.05)               | 21 (22.11)       | 16 (16.84)            |
| Irritability                   | 0                        | 70 (76.09)       | 22 (23.91)            | 22 (23.16)               | 67 (70.53)       | 6 (6.32)              |
| Anxiety                        | 3 (3.26)                 | 65 (70.65)       | 24 (26.09)            | 12 (12.63)               | 83 (87.37)       | 0                     |
| Physical and mental exhaustion | 0                        | 12 (13.04)       | 80 (86.96)            | 0                        | 19 (20)          | 76 (80)               |
| Urogenital                     |                          |                  |                       |                          |                  |                       |
| Sexual problems                | 0                        | 34 (36.96)       | 58 (63.04)            | 0                        | 12 (12.63)       | 83 (87.37)            |
| Bladder problems               | 31 (33.70)               | 55 (59.78)       | 6 (6.52)              | 13 (13.68)               | 60 (63.16)       | 22 (23.16)            |
| Vaginal dryness                | 0                        | 74 (80.43)       | 18 (19.57)            | 0                        | 9 (9.47)         | 86 (90.53)            |



**Figure 1:** Mean total score of peri-and postmenopausal women on MRS. MRS = Menopause Rating Scale

Common menopausal symptoms in India vary when compared to the West. There are variations within different regions of the country. [16-18] These diversities occur because women experience reductions in estrogen levels in a wide variety of ways with greater interindividual variation. [23,24]

The mean age at menopause for the postmenopausal group observed in our study was 45.29 (2.17) years, which is lower than the mean age at menopause in Caucasians, but it was within the normal range for the Indian population.<sup>[12]</sup>

This study was undertaken to describe the menopausal symptoms in terms of prevalence and severity in the treatment seeking women. The assessment tool used in our study was the MRS, which is widely tested and accepted internationally.<sup>[18]</sup> The English version of the MRS questionnaire was used. Although it is a self-administered questionnaire, the questions were translated to the patients in the local language and correct response was recorded. This was done because majority of the patients did not understand English. MRS is composed of 11 most commonly experienced symptoms and each symptom is given a score from 0 (none) to 4 (very severe). The symptoms are further grouped into three subscales. The somatic subscale includes scores of hot flashes.

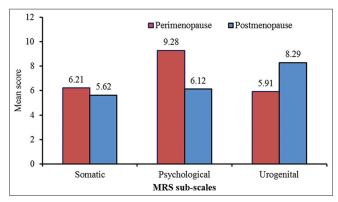


Figure 2: Mean score of subscales of peri-and postmenopausal women on MRS

heart discomfort, sleep problems, and joint and muscular discomfort. The psychological subscale adds up scores of depressive mood, irritability, anxiety, and physical and mental exhaustion. Sexual problems, bladder problems, and dryness of vagina are included in the urogenital subscale.<sup>[16-18]</sup>

The mean total score of the symptoms in both the groups were comparable at 21.4 (5.11) and 20.03 (3.99) for peri- and postmenopausal, respectively and there was no significant difference between the total scores of the subscales.

# Somatic subscale

In the present study, 112 (40.1%) women reported experiencing episodes of hot flashes, sweating, and/or night sweats in the preceding 4 weeks. Prevalence of vasomotor symptoms shows wide variation throughout the world. Studies in the Western population report a higher prevalence up to 75%, while a study in Malaysia reported a prevalence (41.6%) similar to our study. [7-11,22] Even in India, there are wide variations in prevalence of hot flashes during menopause in different regions. Sharma *et al.*, reported a higher prevalence (53.86%) of vasomotor symptoms in a study done in Northern India, while Shah *et al.*, had reported only 19% of women in Mumbai complaining of hot flashes. [13-15]

Among the 92 perimenopausal women interviewed, 61 subjects (66.3%) reported experiencing episodes of hot flashes and/or nightsweats and 28 (35.87%) had severe to very severe symptoms. Though 46 postmenopausal women (52.63%) still reported hot flashes in the past 4 weeks, these were mostly mild to moderate in nature. Similar observations were made in the Menopause Epidemiology (MEPI) study. They reported that 79% of perimenopausal women and 65% of postmenopausal women experienced hot flashes.<sup>[9]</sup> The data by Study of Women's Health Across the Nation (SWAN) also indicated that hot flushes were more frequently reported by women in the late perimenopause.<sup>[25]</sup>

Hot flashes are believed to result from the brain's response to diminished estrogens and estrogen fluctuations that occur during the menopausal transition. With time as the fluctuations decrease, so does the severity of the hot flashes. Besides hormone levels, ethnicity, climate, diet, lifestyle, smoking, and their attitude towards menopause also affect the prevalence of vasomotor symptoms. [20-26]

Ninety-three women (49.73%) in our study reported that they had sleep problems such as difficulty in falling asleep, waking up through the night, or waking up early. The frequency of sleep disturbances were comparable between the two groups, though they were more severe in the perimenopausal group compared to the postmenopausal group. But this was statistically not significant. These findings were found to correspond to findings done in other studies in Indian, Asian, as well as Caucasian women.[3,8,13,27] The Medical Research Council National Survey of Health and Development (NSHD) identified that menopausal transition and its associated symptoms especially night sweats were associated with trouble initiating sleep and sleep fragmentation. To add to this, sleep disturbances may occur independently of menopause in postmenopausal women as nocturia, depression and stress increase with age and may disturb sleep.[28]

All the women interviewed in our study complained of rheumatic complaints like muscle and joint pains. While only 46.74% of perimenopausal women had severe to very severe symptoms, it rose markedly to 90.53% women reporting such severity in the postmenopausal group. This statistically significant (P < 0.001) increase in severity can be attributed to worsening of menopause-linked osteoporosis. In similar demographic studies, joint pains and body ache was found to be the commonest menopausal complain in the Indian population unlike the West. [12-15,29] This has been attributed to poor diet and low calcium intake by women in the youth and lack of physical exercise. [12]

#### **Psychological subscale**

Perimenopausal women had 35% higher psychological score than postmenopausal women indicating higher

frequency and severity of symptoms (P < 0.001). This decrease in symptom is attributed to the decrease in the fluctuation of estrogen levels. The importance of estrogen in cognition has been demonstrated by Jacob and colleagues. The most consistent symptom in both the groups was physical and mental exhaustion, but the severity varied. It was observed that 80 perimenopausal women (86.96%) complained of severe to very severe symptoms as opposed to 76 postmenopausal women (80%). Physical and mental exhaustion was also found to be one of the commonest findings in other studies done in the Indian population.  $^{[11,13,14]}$ 

It has been suggested that during a hot flush, blood flow decreases to the hippocampus, possibly impairing memory and cognition. The severity of the symptoms of irritability, anxiety and depression also decreased with progressing age. Besides fluctuating estrogen levels, another reason for depression and anxiety could be apprehension towards menopause. The Melbourne Women's Midlife Health Project carried out a large-scale study, the results of which indicated that depression scores were higher for women who were in the menopause transition stage (i. e., had not reached final menstrual period) or who had experienced surgical menopause. [33]

### **Urogenital subscale**

Postmenopausal women had 28% higher urogenital score than perimenopausal women (P = 0.008). As the frequency of symptom was similar in both the groups, the higher score of urogenital scale in postmenopausal women was attributed to more severe symptoms among them compared to the perimenopausal women. Similar distribution of urogenital symptoms was also documented by other studies.<sup>[3,8,11]</sup>

All the women in our study reported a decrease in libido, sexual activity and satisfaction. Seventy percent of perimenopausal women also complained of having difficulty in urination, increased frequency, and bladder incontinence. The same was reported by 87% of postmenopausal women. However, bladder problems were more troublesome among the postmenopausal women with 23.1% reporting severe to very severe symptoms compared to 6.52% perimenopausal women with similar severity. 90.53% of the postmenopausal women reported severe to very severe vaginal dryness compared to 19.57% in the perimenopausal group.

As the women progress in postmenopausal age, estrogen levels further falls and it results in vaginal atrophy, dryness, and other urogenital symptoms. Changes in the vaginal environment after menopause predisposes to urinary tract infection (UTI). Recurrent UTI in postmenopausal women are associated with urinary incontinence, cystocele, and increased post-void residual volume.

Increasing awareness, lower age of menopause in India, and the added burden of surgical menopause has made the woman seek therapy for a quality life. Healthcare providers need to tailor the therapy according to the most prominent complaint. Perimenopausal women with prominent vasomotor symptoms and psychological symptoms are most likely to benefit from systemic hormone replacement therapy (HRT).<sup>[2]</sup> Other alternative therapies have also been tried for the classical presentation of vasomotor symptoms with some success. These alternative therapies are most likely to succeed in perimenopausal women instead of postmenopausal women in whom hot flashes are not of much concern. The main concern of postmenopausal women is the urogenital problems for which local estrogen cream is the most judicious therapy. Also, in postmenopausal women, worsening joint and muscle pain deserves special attention from the healthcare provider.

The limitation of our study was small sample size. Moreover, the study was done in patients with symptoms severe enough to warrant treatment. Thus, the result cannot be extrapolated to the population at large. The results are only to guide in selecting the best form of therapy. MRS questionnaire is a self-administered questionnaire, but was administered by face-to-face interview in the local language. Some bias is to be expected due to this also.

#### CONCLUSION

During menopausal transition there are a lot of fluctuations in the hormone levels (especially estrogen) and thus women experience many symptoms and conditions. However, the influence of this fluctuation varies from one woman to another. The present study using the MRS showed that the mean age of menopause was 45.29 (2.17) years. Study of the 11 symptoms on the MRS found that these symptoms were more common and severe during the perimenopausal phase. Fatigue, depression, anxiety, hot flashes, and sexual disturbances were the common symptoms that appeared first during the menopausal transition. As the age advanced and women progressed in the postmenopausal stage, the psychological symptoms of depression, irritability, and sleep disturbances decreased; while the urogenital symptoms, fatigue, and generalized body ache become more prominent.

#### REFERENCES

- Singh A, Arora AK. Profile of menopausal women in rural north India. Climacteric 2005;8:177-84.
- In: Edmond DK, editor. Menopause and the Postmenopausal woman. Dewhurst's Textbook of Obstetrics and Gynecology. 7<sup>th</sup> ed. Blackwell publishing; 2007. p. 492.
- Dutta R, Dcruze L, Anuradha R, Rao S, Rashmi MR. A population based study on the menopausal symptoms in a rural area of Tamil Nadu, India. J Clin Diagn Res 2012;6:597-601.

- Burger HG, Dudle EC, Hopper JL, Groome N, Guthrie JR, Green A, et al. Prospectively measured levels of serum follicle-stimulating hormone, estradiol and the dimeric inhibins during the menopausal transition in a population based cohort of women. J Clin Endocrinol Metab 1999;84:4025-30.
- Santoro N, Brown JR, Adel T, Skurnick JH. Characterization of reproductive hormonal dynamics in the perimenopause. J Clin Endocrinol Metab 1996;81:1495-501.
- Burger HG, Hale GE, Robertson DM, Dennerstein L. A review of hormonal changes during the menopausal transition: Focus on findings from the Melbourne Women's Midlife Health Project. Hum Reprod Update 2007;13:559-65.
- Bachmann GA. Vasomotor flushes in menopausal women. Am J Obstet Gynecol 1999;180:S312-6.
- Rahman SA, Zainuddin SR, Mun VL. Assesment of menopausal symptoms using modified Menopause Rating Scale (MRS) among middle age women in Kuching, Sarawak, Malaysia. Asia Pac Fam Med 2010;9:5.
- 9. William RE, Kalilani L, DiBenedetti DB, Zhou X, Granger AL, Fehnel SE, *et al.* Frequency and severity of vasomotor symptoms among peri- and postmenopausal women in the United States. Climacteric 2008;11:32-43.
- 10. Blümel JE, Chedraui P, Baron G, Belzares E, Bencosme A, Calle A, *et al.* Collaborative Group for Research of the Climacteric in Latin America (REDLINC). A large multinational study of vasomotor symptom prevalence, duration, and impact on quality of life in middle-ages women. Menopause 2011;18:778-85.
- Palacios S, Henderson VW, Siseles N, Tan D, Villaseca P. Age of menopause and impact of climacteric symptoms by geographical region. Climacteric 2010;13:419-28.
- Unni J. Third consensus meeting of Indian Menopausal Society (2008):
   A Summary. J Midlife Health 2010;1:43-7.
- 13. Sharma S, Tandon VR, Mahajan A. Menopausal symptoms in urban women. JK Sci 2007;9:13-7.
- Bagga A. Age and symptomatology of menopause: A case study. Obstet Gynecol Today 2004;11:660-6.
- Shah R, Kalgutkar S, Savardekar L, Chitlang S, Iddya U, Balaiah D. Menopausal symptoms in urban Indian women. Obstet Gynecol Today 2004;11:667-70.
- Heinemann K, Ruebig A, Potthoff P, Schneider HP, Strelow F, Heinemann LA, et al. The Menopause Rating Scale (MRS): A methodological review. Health Qual Life Outcomes 2004;2:45.
- 17. Schneider HP, Heinmann LA, Rosemeier HP, Potthoff P, Behre HM. The Menopausal Rating Scale (MRS): Comparison with kupperman index and quality-of-life scale SF-36. Climacteric 2000;3:50-8.
- Heinmann LA, Potthoff P, Schneider HP. International versions of the Menopausal Rating Scale (MRS). Health Qual Life Outcomes 2003;1:28.
- Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, et al. STRAW+10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop – 10: Addressing the unfinished agenda of staging reproductive aging. Fertil Steril 2012;97:843-51.
- Sherman BM, Korenman SG. Hormonal charachteristics of the human menstrual cycle throughout reproductive life. J Clin Invest 1975;55:699-706.
- 21. Gruber CJ, Tschugguel W, Schneeberger C, Huber JC. Production and actions of estrogens. N Engl J Med 2002;346:340-52.
- Green R, Polotsky AJ, Wildman RP, McGinn AP, Lin J, Derby C, et al. Menopausal symptoms within a Hispanic cohort: SWAN, the Study of Women's Health Across the Nation. Womens Health (Lond Engl) 2009;5:127-33.
- Randolph JF Jr, Sowers M, Bondarenko IV, Harlow SD, Luborsky JL, Little RJ. Change in estradiol and follicle-stimulating hormone across the early menopausal transition: Effects of ethnicity and age. J Clin Endocrinol Metab 2004;89:1555-61.

- 24. Woods NF, Cray L, Mitchell ES, Herting JR. Endocrine biomarkers and symptom clusters during the menopausal transition and early postmenopause: Observations from the Seattle Midlife Women's Health Study. Menopause 2014;21:646-52.
- Thurston RC, Joffe H. Vasomotor symptoms and menopause: Finding's from the study on Women's Health across the Nation. Obstet Gynecol Clin North Am 2011;38:489-501.
- 26. Gold EB, Block G, Crawford S, Lachance L, FitzGerald G, Miracle H, *et al.* Lifestyle and demographic factors in relation to vasomotor symptoms: Baseline results from the Study of Women's Health Across the Nation. Am J Epidemiol 2004;159:1189-99.
- 27. Kravitz HM, Ganz PA, Bromberger J, Powell LH, Sutton-Tyrrell K, Meyer PM. Sleep difficulty in women at midlife: A community survey of sleep and the menopausal transition. Menopause 2003;10:19-28.
- Tom SE, Kuh D, Guralnik JM, Mishra GD. Self-reported sleep difficulty during the menopausal transition: Results from a prospective cohort study. Menopause 2010;17:1128-35.
- Gao HL, Lin SQ, Wei Y, Chen Y, Wu ZL. The effect of age and menopausal status on musculoskeletal symptoms in Chinese women

- aged 35-64 years. Climacteric 2013;16:639-45.
- Jacobs DM, Tang MX, Stern Y, Sano M, Marder K, Bell KL, et al. Cognitive function in nondemented older women who took estrogen after menopause. Neurology 1998;50:368-73.
- 31. Yaffe K, Sawaya G, Lieberburg I, Grady D. Estrogen therapy in postmenopausal women: Effects on cognitive function and dementia. JAMA 1998;279:688-95.
- 32. Shumaker SA, Legault C, Rapp SR, Thal L, Wallace RB, Ockene JK, et al. Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: The Women's Health Initiative Memory Study: A randomized controlled trial. JAMA 2003;289:2651-62.
- Henderson VW. Gonadal hormones and cognitive aging: A midline perspective. Womens Health (Lond Engl) 2011;7:81-93.

How to cite this article:\*\*\*

Source of Support: Nil, Conflict of Interest: None declared