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### ABSTRACT

*Background:* Menopausal transition may occur between 45 and 55 years old and take 3–9 years. During this transition, the hormonal changes may contribute to the physical and psychological complaints in women. One of the psychological complaints is a sign of depression. However, not all of the women will experience those complaints.

*Objective:* To assess the relationship between depression in menopause transition and other menopausal symptoms and factors contribute to depression among Indonesian people.

*Methods:* Cross-sectional study on 133 female subjects between 45 and 55 years old. Depression measured using Beck Depression Inventory-II (BDI-II), and menopausal symptoms were collected using Menopause Rating Scale (MRS). The comparison and relation were assessed for every aspect regarding depression and menopausal symptoms.

*Results:* Out of 133 subjects, depression was found in 17 subjects (12.8%). Somato-vegetative symptoms were complained by 50.4% and urogenital symptoms by 75.9% subjects. There was significant correlation between depression and somato-vegetative (p = 0.008) as well as urogenital complaints among women who underwent menopause transition (p = 0.016). These findings were consistent with previous studies.

*Conclusion:* Depression on menopausal transition significantly correlated with somato-vegetative and urogenital symptoms among women. Future investigations should be conducted with a cohort design to observe mood alterations during the menopause transition.

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## 1. Introduction

Depression is a common psychological condition and estimated to affect 350 million worldwide population [1]. Depression may decrease work performance, interpersonal relationship, financial status, and the appearance of suicide ideation. Although it is a psychological condition, depression may implicate to physical wellbeing and increasing morbidity and mortality [2,3].

Depression is twice more common in women compared to men. This high risk in women may be caused by hormonal changes in condition such as puberty, pregnancy, and menopausal transition [4].

Menopausal transition is a period when women undergo irregular menstruation and cessation of menstrual cycle [5]. Menopause

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transition may occur up to three to nine years in the midlife around 45–55 years old [6]. In the midlife, a woman may experience several health problems, changes in social function, work and family thus contribute in psychological condition [7].

Menopausal transition is marked by fluctuation of sex-steroid hormones and symptoms of vasomotor, psychic, and psychosomatic [8–10]. Still in controversy, what is the most complained of menopausal symptoms among menopausal women? National Institute of Health stated that vasomotor symptoms (hot flushes and night sweating), vaginal dryness, and sleep problem are the most common menopausal symptoms. Mood disorder including depression is not common in menopausal symptoms, although it often coincides with menopausal transition. Previous studies showed that there might be associations between depression and other menopausal symptoms and vise versa. However, it is still not clear whether the causation is strongly related or merely coincidental [11,12].

In this study, we will focus on menopausal transition toward depression symptoms. Then, depression symptoms will be associated with other menopausal symptoms during the menopausal

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transition. The study observing symptoms of menopausal transition including depression are still limited in Indonesia thus encourages the authors to conduct this study.

## 2. Material and methods

This is a cross sectional study to assess depression and other menopausal symptoms in women forty-five to fifty-five years old. We collected data consecutively on one hundred and fifty subjects starting from February until May 2016. The study was conducted in Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia.

Subjects were enrolled based on inclusion and exclusion criteria. The inclusion criteria were women with 45–55 years old and willing to participate (informed consent obtained). The exclusion criteria were women with a history of gynecological condition that caused earlier menopause (before 45 years old); having mentally ill condition or another psychological condition (especially mood disorder); and/or having any illness that may impact menopausal symptoms (malignancy, thyroid disease, autoimmune diseases, heart diseases). Sample size was calculated using the formula for estimated proportion in infinite number of population. We used confidence level of 95% and power of study of 90%. The minimum number of samples required was one hundred subjects.

Data collected in this study were primary data, which collected via questionnaires. Every subject had been informed of the purposes of this study, the procedures, and data collected. Informed consents had been obtained from all the subjects participating in this study. Every subject had agreed to share data collected regarding the publication of this study. The ethical committee of Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia, had approved this study.

Every subject was asked to fill three questionnaires consist of baseline data, Beck Depression Inventory-II (BDI-II), and Menopause Rating Scale (MRS). BDI-II was used to identify symptoms and diagnosis of depression among menopausal women. MRS was used to assess menopausal symptoms (especially somatovegetative and urogenital symptoms).

BDI-II consists of twenty-one questions characterizing symptoms of depression. This tool has been used in medical or psychiatric practice around the world. Subjects may choose one of four possible boxes based on her condition in each question. For the purpose of this study, BDI-II score fourteen or more was considered to be depressive [13].

MRS was developed and validated some years ago aiming at establishing an instrument to measure health-related quality of life that can easily complete by women. Three dimensions of symptoms were identified using this questionnaire including somatovegetative (vasomotor), psychological, and urogenital factors. MRS consists of 11 items of questions, 4 questions each to assess somato-vegetative and psychological symptoms and 3 questions to assess urogenital symptoms. The subjects provide her personal perception by checking one of five possible boxes of severity [14].

For the purpose of this study, we categorize each somatovegetative and urogenital symptoms into no/little symptoms, mild symptoms, moderate symptoms, and severe symptoms from MRS score. Women who had somato-vegetative symptoms score 3 or more; psychological symptoms score 2 or more; and urogenital symptoms score 1 or more were considered having positive menopausal symptoms. Based on somato-vegetative domain participants were divided into no/little symptoms (0–2); mild symptoms (3–4); moderate symptoms (5–8); and severe symptoms ( $\geq$ 9). Last, based on urogenital domain participants were divided into no symptom (0); mild symptoms (1); moderate symptoms ( $\geq$ -3); and severe symptoms ( $\geq$ 4). Data was analyzed with SPSS software for Windows version 22. To exhibit a correlation between depression (BDI-II score) and menopausal symptoms, we used Spearmen test or Pearson correlation test depended on the distribution of data. To compare the difference of each group (depressive and normal subject), we used Chi-square or Fisher exact test.

#### 3. Results

One-hundred and fifty subjects were enrolled in this study. Seventeen subjects were excluded from the study due to exclusion criteria, hence total of one-hundred and thirty-three subjects were included in the analysis.

From 133 subjects, depression was found in seventeen subjects (12.8%). According to baseline data, normal and depressive subjects exhibited no difference between two groups in age of menarche, marital status, occupation, education, and monthly income (p > 0.05). Detailed of baseline characteristics between the two groups can be seen in Table 1.

Assessment of menopausal symptoms using MRS found 50.4% and 75.9% of subjects had somato-vegetative and urogenital symptoms, respectively. From the symptomatic women, most of the normal subjects had mild somato-vegetative symptoms and moderate to severe urogenital symptoms. Compared to depressive subjects, most of the subjects had moderate somato-vegetative symptoms and severe urogenital symptoms (Fig. 1). There was significant correlation between depression and somato-vegetative (p < 0.05; r = 0.236) as well as urogenital complaints (p < 0.05; r = 0.215) among women who underwent menopause transition. Distribution of menopausal symptoms among subjects can be seen in Table 2.

We also correlate BDI-II scores with somato-vegetative and urogenital scores (from MRS) using pearson correlation test (normal distribution of data). There was significant positive correlation between BDI-II scores and MRS scores for somato-vegetative (p < 0.05; r = 0.468) and urogenital complaints (p < 0.05; r = 0.474).

## 4. Discussion

This study was conducted to assess the relationship between depression in menopause transition and other menopausal symptoms and factors contribute to depression among Indonesian people. Menopausal symptoms observed in this study consisted of somato-vegetative and urogenital symptoms. Factors assumed to contribute in depression including monthly income, education, and occupational status.

Table 1				
Baseline	characteristics	of	sub	iects

Baseline data	Normal	Depression	P-Value
Age (Mean and SD) Age of Menarche (Mean and SD)	50.75 (3.37) 13.39 (1.25)	49.98 (3.35) 13.76 (1.25)	0.323 <sup>a</sup> 0.25 <sup>a</sup>
Monthly income Low income High income	56 (48.3%) 60 (51.7%)	10 (58.8%) 7 (41.2%)	0.417 <sup>b</sup>
Education Low educated Highly educated	47 (40.5%) 69 (59.5%)	9 (52.9%) 8 (47.1%)	0.333 <sup>b</sup>
Occupation status Working Not working Total	24 (20.7%) 92 (79.3%) 116 (87.2%)	4 (23.5%) 13 (76.5%) 17 (12.8%)	0.756 <sup>c</sup>

<sup>a</sup> Independent T-test.

<sup>b</sup> Chi-square test.

<sup>c</sup> Fisher's exact test.



III Mild symptoms Moderate symptoms Severe symptoms

Fig. 1. Domain of menopausal symptoms in normal and depressive subjects.

Table 2 Distribution of menopausal symptoms among subjects.

	Normal	Depression	P-Value
Somato-Vegetative Symptoms Scores (Mean and SD)	2.97 (2.62)	4.71 (2.44)	0.011 <sup>°a</sup>
No/little symptoms Mild symptoms Moderate symptoms Severe symptoms	62 (53.4%) 28 (24.1%) 23 (19.8%) 3 (2.6%)	4 (23.5%) 4 (23.5%) 8 (47.1%) 1 (5.9%)	0.008 <sup>*b</sup>
Urogenital Symptoms Scores (Mean and SD)	2.17 (2.06)	3.65 (2.18)	0.007 <sup>*a</sup>
No/little symptoms Mild symptoms Moderate symptoms Severe symptoms	31 (26.7%) 27 (23.3%) 29 (25%) 29 (25%)	1 (5.9%) 2 (11.8%) 5 (29.4%) 9 (52.9%)	0.016 <sup>°b</sup>
BDI-II Scores (Mean and SD)	4.01 (3.62)	18.53 (4.09)	0.000 <sup>*a</sup>

Significant at <0.05.

Independent T-test.

b Spearmen's rho correlation test.

From one-hundred and thirty-three subjects, depression was found in seventeen subjects. Neither in depression group nor in the normal group was found to be significantly different in monthly income, education level, and occupational status.

Menopausal transition is a period of hormonal changes marked by declining of ovarian hormones production. Ovarian hormones level during this transition phase may not be predictable and declined gradually hence contributing to menopausal symptoms [15].

Previous studies showed the relationship between menopausal transition and depression [16-18]. Depression in menopausal transition is hypothesized due to estrogen deficiency. Estrogen deficiency may reduce serotonin activities in the brain. Diminished serotonin levels hence contribute to alteration of mood such as depression [15]. Estrogen was known to interact with serotonergic system through estrogen-beta receptors. Estrogen will reduce monoamine oxidase level that will increase serotonin level [19].

Study conducted by Cohen et al. showed that the risk of developing depression on menopausal transition was increased by the appearance of vasomotor symptoms and adverse life events. If menopause women have both of them, the chance of getting depression would be much higher with odd ratio up to 2.5 [18]. In this study, we found a significant association between depression and somato-vegetative symptoms as well as urogenital symptoms. There was a trend of significant increased of BDI-II scores followed by increased by somato-vegetative and urogenital symptoms scores using MRS.

There are many factors that may contribute to depression in menopausal transition. The chance of getting depression may be increased due to several aspects including adverse or stressful life events, surgical menopause, history of depressive mood disorder and menopausal symptoms itself such as vasomotor symptoms [16-18,20,21].

Previous studies also showed the relationship between vasomotor symptoms and depressive symptoms during menopausal transition [16,18,22,23]. Besides, sleeping problem was associated with depressive symptoms in menopausal transition. Still not clear whether vasomotor symptoms and depression were linked via biological mechanisms, social and psychological impact of vasomotor symptoms, or depression that cause those symptoms. The previous study was stated that this relationship was due to "domino effect" which vasomotor symptoms may cause sleeping problems hence increasing the likelihood to develop depression [24]. Complexities of this relationship show a necessity to conduct further investigations [25]. However, there was no previous study showing the associations between depression and urogenital symptoms in menopausal transition [26].

Need to be considered, mood alterations during menopause transition may be caused by several variables such as increased sensitivity to events that influenced by hormonal level declination, change in socioeconomic status and or marriage, cultures, lifestyles, education level and history of depression itself [15].

Several trials have documented the efficacy of psycothropic medications (antidepressant agents) to alleviate mood and other menopause related symptoms in perimenopausal and postmenopausal. Although the mechanisms by which antidepressants alleviates menopausal symptoms remain unknown, recent data suggest a potential effect via norepinephrine and serotonin systems. Hence the effects of these agents on menopausal symptoms (especially somato-vegetative symptoms) could therefore occur via modulation of noradrenergic circuitry [27,28]. In addition, evidence supports a possible window of opportunity for hormonal treatments to manage depressive symptoms as well. Estradiol can decrease the activity of monoamine oxidases, which are enzyme involved in serotonin degradation, thus reducing the symptoms of depression [29]. Further studies investigating this phenomenon might be a great value to better understand and overcome the menopausal symptoms in menopausal transition.

Clinical implication that can be implied from this study is every woman during menopause transition may be benefited from depression screening to detect early symptoms of depression. Early recognition of depression may significantly improve their quality of life during menopausal transition as it can be treated earlier.

Strength of this study is the subject was normal women without history of mood disorders, early menopause and or surgical menopause. In addition, this is the study to correlate menopausal symptoms and depression in Indonesian women, which is still limited in Indonesia. Limitation of this study is the data was only taken in one time hence we couldn't identify mood changes before and during the menopausal transition. In the future investigation, the study may be conducted in cohort design to observe mood alterations before, during and after menopause transition.

#### 5. Conclusion

This study was found that there was statistically significant positive correlation between depression on menopausal transition and somato-vegetative symptoms as well as urogenital symptoms. There was no statistically significant different for education level, occupational status and monthly income with depression. Further studies should be encouraged to assess the role of antidepressants toward somato-vegetative and/or urogenital symptoms in menopausal transition.

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### **Conflict of interest**

None to declare.

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