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Clustering Iranian women according to their menopausal severity symptoms and exploring the factors associated with severe categories, using baseline category logit model

Fahimeh Hoseinzadeh¹, Habibollah Esmaily^{1*}, Sedigheh Ayatiafin² and Azadeh Saki^{1*}

Abstract

Introduction Many studies reported that the factors associated with the intensity of menopausal symptoms vary according to race, culture, and ethnicity. Different instruments, measure severe menopausal symptoms. The present study aims to classify Iranian women between 42 and 60 years according to the similarity of menopausal severity symptoms and then find the risk factors related to allocating in severe symptoms groups.

Method In this cross-sectional study, 664 women aged 42–60, living in Mashhad, Iran were collected. The Menopause Severity Symptoms Inventory (MSSI-38) was used to collect information about menopausal symptoms. K-Means clustering algorithm was applied to classify women with different menopausal symptoms in separate groups. The baseline category logit model and ANOVA were used to find the associated factors and covariates with clusters.

Result K-Means clustering algorithm, extracted three major clusters based on different menopausal symptoms. The first cluster involved 301 (45%) women with mild symptoms, the second was a cluster of moderate symptoms women with size 131 (20%). The remaining 232 (35%) of women were placed in the third cluster. The baseline category logit model showed that Compared to Cluster 1, Cluster 2 is associated with a higher underlying diseases (OR = 1.51, P -value = 0.03), lack of physical activity (OR = 1.79, P -value = 0.003), having more than five pregnancies (OR = 2.11, P -value = 0.017), and being peri menopause (OR = 1.71, P -value = 0.03). In contrast, Cluster 3 shows an even stronger association with underlying diseases (OR = 3.71, P -value < 0.001), physical activity (OR = 2.46, P -value = 0.001), insufficient income (OR = 3.43, P -value < 0.001, and being peri menopause (OR = 2.09, P -value = 0.029) or post menopause (OR = 2.02, P -value = 0.044) when compared to Cluster 1.

Conclusion Based on these findings, women with underlying diseases, varying levels of physical activity, different income levels, different number of pregnancies, and menopause status in the moderate (Cluster 2) and severe symptomatic groups (Cluster 3) exhibited significant differences compared to those in the mild symptomatic group

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(Cluster 1). These results underscore the necessity for targeted interventions, such as promoting physical activity and providing mental health support, to alleviate menopausal symptoms. Additionally, further research is essential to identify the causal factors contributing to these symptoms, which could lead to improved care and health policies for women experiencing menopause.

Keywords Cluster analysis, K-Means algorithm, Menopausal Severity Symptoms (MSSI-38), Baseline category logit model

Introduction

Menopause is a natural physiological event that occurs in the lives of all women. When it occurs normally, it is not attributable to any pathological or physiological cause [1]. Menopause is associated with hormonal changes in the body and menopausal symptoms are due to decreased ovarian function, the aging process, and other environmental factors [2, 3].

The age of menopause may vary from one population to another. The mean age of menopause is about 51 years in industrial countries [4, 5]. The mean age at menopause was reported in a study as 50.4 years among Iranian women in 2004 [1]. In the recent conducted study by Pasokh et al., the age at natural menopause was estimated to be 48.95 years among postmenopausal women in Kharameh, Iran [6]. Also, In a population-based study the mean age at natural menopause was 48.31 [7].

The findings show that compared to other societies, menopause age in Iran is relatively within earlier ages. Some studies reported the age at menopause for Asian women is between 49 and 50 years [8, 9].

The bio-medical paradigm focuses on menopause from a physiological point of view. From the biological model's point of view, the mean and standard deviation of natural menopause age is 51 ± 8 years. That is explained in terms of disparities in the initial determination of non-growing follicles or the rate of non-growing follicle depletion [10].

In Western countries, menopausal symptoms such as hot flashes and vaginal dryness are considered the main climacteric complaints [11]. In other cultures, particularly in Islamic and Asian countries, menopausal symptoms can differ significantly from those experienced by Western women. These differences are influenced by cultural attitudes and beliefs regarding menopause, as well as socioeconomic and lifestyle factors. As a result, women in these cultures may develop negative perceptions of the menopausal experience [12].

Self-care plays a crucial role in women's health during menopause. Engaging in self-care activities can help women manage menopausal challenges and enhance their quality of life. However, some studies indicate that many Iranian women do not practice sufficient self-care during this phase [13, 14].

In Simbar et al. research, multiple linear regression analysis revealed that a husband's education level and

family size are significant predictors of self-care practices among postmenopausal Iranian women [15].

In a study conducted by Dehghan et al., it was found that the severity of menopausal symptoms, as well as scores in the somatic-vegetative and urogenital domains, were higher among users of complementary and alternative medicines (CAM) in postmenopausal women in Southeast Iran compared to non-CAM users [16].

In a study by racial distribution of Chinese, Malay and Indian, hot flushes (17.6%), vaginal dryness (20.7%) and night sweats (8.9%) were less commonly reported than somatic symptoms [17]. Nevertheless, in a study conducted by Pinar et al., which evaluated menopausal symptoms in Turkish and German women, it was found that for Turkish women, the prevalence of urogenital symptoms rises with age. In contrast, for German women, an increase in age is associated with a rise in somatic, psychological disease, and overall symptoms [18]. The symptoms associated with menopause among Iranian women were hot flushes, mood swings, vaginal dryness, sleep problems, night sweats, memory loss, urinary symptoms, palpitation, anxiety, joint and muscle pain, depression, irritability, decreased libido, fatigue, and weight gain [19–22]. In a systematic review, among Iranian women, the prevalence of hot flashes varied from 32.3 to 69.65% and the prevalence of night sweats varied from 12.8 to 55.5 [23].

As life expectancy increases, women are spending more years in the postmenopausal period, meanwhile menopause impacts various aspects of a woman's life including physical, mental, emotional, and social functioning, so it significantly affects women's quality of life [19, 24]. Alison Kochersberger et al., suggest that understanding and addressing social, cultural, and economic factors are crucial to reducing disparities in menopausal symptoms but, there are still large knowledge gaps in race, ethnicity, and cultural differences in menopausal health [25]. So far, various tools have been developed and employed to measure the frequency of menopausal symptoms [26, 27]. Several of these tools have been validated through research related to menopause. Additionally, a novel tool, the 38-MSSI questionnaire, has been introduced to assess and quantify the frequency and severity of menopause symptoms using a 5-point Likert scale [28].

Understanding similarities and differences among women's menopause severity symptoms surrounding

menopause, improves the health policymakers' knowledge of interventions on care and promotes lifestyles that may decrease symptoms and increase quality of life.

Clustering is a machine-learning technique employed to group similar data points [29]. The objective is to partition a set of objects into clusters, in which the objects within a cluster exhibit greater similarity to one another than to those in other clusters. By employing clustering techniques, researchers can discern patterns, relationships, and similarities among various risk factors, ultimately providing valuable insights for understanding the impact of these factors on menopausal symptomatology [29]. Furthermore, this approach aids in identifying specific groups of individuals who may be more susceptible to experiencing severe symptoms, thereby facilitating targeted interventions and personalized healthcare strategies [29].

In the context of menopause, clustering analysis can help identify patterns or clusters of symptoms that frequently occur together, as well as the risk factors associated with those clusters [29]. For example, a study using clustering analysis found that women in the highly symptomatic classes more frequently rated their health as fair to poor compared to women in the least symptomatic classes [30]. This suggests that clustering analysis can help identify women who are at a higher risk of experiencing poor health outcomes during menopause. Another study using clustering analysis found that women with metabolic syndrome experienced different symptom clusters compared to women without metabolic syndrome [31]. This suggests that clustering analysis can help identify women who are at a higher risk of experiencing complex symptoms associated with menopause transition and metabolic syndrome.

Cluster analyses can be conducted either by grouping people or by grouping symptoms. Cluster analyses by people help identify specific risk groups, whereas cluster analyses by symptoms can assist in identifying the connections between different co-existing symptoms. However, most existing cluster analyses have focused on grouping symptoms alone [29, 32]. For instance, In the study of Cray, Woods, and Mitchell, the researchers explored mood, vasomotor, and pain components in menopausal symptoms [33]. In the study of Mishra and Kuh (2018), four clusters were extracted through hierarchical cluster analyses [34]. The study of Eun-Ok Im et al., was aimed to identify clusters of midlife women by their cognitive symptoms and to examine racial/ethnic differences in the clusters. In a study four clusters were extracted [35]. Masakazu Terauchi et al., performed a principal component analysis followed by a hierarchical cluster analysis of the responses to 9 physical and 12 psychological items on the questionnaire and generate 4 clusters [36].

Due to the variety of menopausal symptoms among Iranian women, this exploratory study to find and clustered similarity and variability in menopause severity symptoms was conducted. To the best of our literature reviews, no study used the clustering of menopause symptoms in Iran. Thus the purpose of the current study is to find the subgroups of Iranian women according to their menopausal severity symptoms measured by MSSSI-38 and conducting baseline category logit model and finding the factors related to allocating in each cluster.

Materials and methods

Study design

This cross-sectional study included 664 women aged 42–60, living in Mashhad, Iran. The information for this study was collected from the five health centers affiliated with Mashhad University of Medical Sciences using multi-stage with stratified, cluster, and simple random sampling.

Study setting

After obtaining permission from Health Deputy of Mashhad University of Medical Science, the researchers and eleven trained assistants completed the research questionnaires. All of assistants were nursing and health group students. One of the research team members trained them how to interview the participants. Research assistants were trained about method of interviewing and importance of participant's privacy. Before conducting the interviews, informed consent was obtained from all of the participants. The questionnaires were then completed through one-on-one interviews.

Participants

In this study, women aged 42 to 60 were included. Participants who had undergone hormone therapy, chemotherapy, or bilateral oophorectomy, as well as those experiencing non-natural menopause, were excluded. Additionally, pregnant and non-native women were also excluded from the study.

Variables

The Menopause Severity Symptoms Inventory (MSSI-38) was used to collect information about menopausal symptoms. The demographic information was obtained by a structural interviewed form which contained age, marital status, education, income, employment status, economic status, household population, physical and psychological health status, and smoking. Additionally, the body mass index (BMI) was measured by recording the height and weight of the individuals at the center. The income of the participants was assessed based on self-declared information and whether it was perceived as sufficient or not. Furthermore, the participants were asked about their

physical activity, including whether they engaged in exercise, the frequency of exercise per week, and the duration of each exercise session. If a woman has regular weekly exercise, her physical activities are considered, yes.

The menopausal status of participants was determined by a self-report method based on STRAW criteria. Pre-menopausal women were identified for not having any changes in their menstrual cycle. Peri menopausal women would report variable cycle length (more than seven days different than usual), or had skipped two or more cycles and had an amenorrhea interval superior to sixty days. Post-menopausal women were confirmed for having at least a twelve-month period of amenorrhea.

The study included underlying disease and psychological problems as a confounding variable that could impact the severity of menopausal symptoms.

MSSI-38 questionnaire

In the study conducted by Pimenta et al. (2006), the primary version of the MSSI-38 consisted of 38 items and 12 factors [28]. According to Hoseinzadeh, (2018), The MSSI utilized in this study consists of 26 items rated on a 5-point Likert scale and seven factors including anxiety, depression, vasomotor, pain in the head and body, pain in the muscles and joints, cognitive impairment, and urinary-genital symptoms [37]. Consequently, the total score for this questionnaire ranges from 26 to 130. For each factor within the questionnaire, the score can vary between the product of 1 and the number of items for that factor (minimum score) and the product of 5 and the number of items for that factor (maximum score). This scoring system allows for a comprehensive assessment of the severity of menopausal symptoms across different dimensions, and seven factors including anxiety, depression, vasomotor, pain in the head and body, pain in muscles and joints, cognitive impairment and urinary-genital symptoms.

Data and sample size determination

The sample size for this study was calculated based on vasomotor symptoms which is the most common symptom with $p=0.42$, prevalence [23]. We consider $d=10\%$, $p=0.042$, precision, and $1-\alpha=0.95$, confidence level, and $z=1.96$, which is the z-statistic for the 95% confidence level in the following formula for random sampling,

$$\dot{n} = \frac{Z_{1-\alpha/2}^2 \times P(1-P)}{d^2} = 531,$$

As our sampling design was stratified cluster sampling, there was Intra-Cluster Correlation (ICC) that could decrease the study precision so, the Design Effect (DEFF) was used to modify the sample size:

$$DEFF = 1.25, \rightarrow n = 1.25 \times 531 = 664$$

The sampling in this study was multi-stage with stratified, cluster, and simple random sampling [35, 36]. Initially, the five major health centers of Mashhad (The center of Khorasan Razavi province in East North of Iran) were treated as strata. The sub-centers of each stratum were considered as clusters. The number of sampling clusters at each stratum to participated in the study was determined using the sampling fraction. Finally, simple random sampling was performed to select the participants in each cluster.

Statistical analysis

To classify women based on their menopause symptoms, the k-means clustering method was utilized. Clustering algorithms leverage the underlying structure of data distributions to define rules for grouping similar data points. The k-means algorithm is a robust unsupervised data mining technique capable of effectively organizing participants into meaningful clusters across various dimensions [38].

Its simplicity and low computational complexity have contributed to the k-means algorithm's widespread use in numerous fields for addressing clustering challenges. In the standard k-means approach, the user must specify the number of clusters (k), which affects the initial selection of cluster centers from the dataset. This requirement can pose difficulties, as the k-means algorithm may converge to a local minimum due to its greedy nature [39]. Consequently, it is recommended to run the algorithm multiple times with different initial cluster center selections for a given k value to increase the chances of achieving optimal clustering outcomes [40]. The Analysis of variance (ANOVA) was used to examine the differences in the menopause symptoms among the clusters.

A baseline category logit model was employed to identify the factors associated with allocation into different clusters. This model was selected due to its appropriateness for the type of dependent variable under investigation, which is categorical with more than two unordered categories. It allows researchers to effectively explore the influential factors and assess the relative importance of various predictors [38]. One of the key advantages of this model is its capability to simultaneously estimate log odds for all pairs of categories, providing a comprehensive view of the relationships among the variables. In constructing the model, only significant predictors with p -values less than 0.10 included. This threshold was chosen to ensure that potentially important predictors were not omitted, while also maintaining a balance between statistical rigor and practical relevance. Results of this model led to enhance the study explanatory power and

ensure that the included variables meaningfully contribute to understanding the clustering dynamics.

Furthermore, the baseline category logit model facilitates the interpretation of results by allowing for comparisons across different categories, which can illuminate how specific factors influence the likelihood of being allocated to particular clusters. This insight is crucial for developing targeted interventions or strategies aimed at addressing the needs of women experiencing menopause symptoms. Overall, the use of the baseline category logit model provides a robust framework for understanding the complex relationships between various factors and their impact on clustering outcomes [38].

Results

Table 1 shows the results of chi-square test and frequency distribution of background characteristics and health status for participating women by their menopause status. The mean age of participants was 50.40 ± 5.5 . Approximately 78% of them had less than a diploma or elementary degree. About 52% of them reported no problem with family income. About 87% were married or partnered, 59% had 1 or 2 children, 55% reported no underlying disease and 86% reported no psychological problem.

Figure 1 displays the distribution of women by age group (42–60 years) at various stages of menopause. The figure indicate a concentration of women aged between 44 and 46, with 79.9% being premenopausal, 57.8% in the peri-menopausal, and 8.5% post-menopausal. The data clearly illustrates an increase in the proportion of menopausal individuals with age; in the over-56 age group, nearly all women have undergone menopause.

The findings show that the most commonly reported symptoms of menopause were pain in muscles and joints (45.2%), followed by anxiety (37.0%) and vasomotor symptoms (41.0%) (Supplementary file 1. Table S1). There were notable variations in the severity of menopausal symptoms among the three groups of women, except for pain in the head and body. Pre-menopausal women demonstrated a significant disparity in menopausal symptom intensity compared to peri and post-menopausal women. Peri-menopausal women only differed from post-menopausal women in vasomotor symptoms.

Table 2 displays the frequencies of items associated with menopausal severity symptom factors. Among the six items contributing to anxiety, the most commonly reported complaints by women were related to feeling tired or lacking energy (56.6%), followed by feeling tense or nervous (54.7%). For the depression factor, the majority of women (36.6%) expressed concerns about experiencing crying spells. Excessive sweating (46.5%) was the most commonly reported complaint linked to the vasomotor factor. For the pain in the head and body, the feeling of tension and pressure on the head or body (25.0%)

was the most frequently reported complaint, followed by headache (24.2%). The pain in muscles and joints (50.9%), and the lower back pain (47.2%) were the common dissatisfaction in the muscular pain dimension. In the difficulty in decreased memory and concentration factor, most individuals experienced difficulty concentrating (28.7%), followed by a sense of loss or lack of memory (27.4%). Concerning the urinary-genital symptoms factor, 26.8% of women reported a loss of sexual interest.

Table 3 displays the associations between predictor variables and clusters using chi-square statistical test. About 45.3% of the participants were categorized into cluster 1 (the low total symptom group); 19.7% were categorized into cluster 2 (the moderate total symptom group); and 34.9% were categorized into cluster 3 (the high total symptom group). There were no significant differences among the three clusters in age, job, husband's job, number of children, and BMI. However, there were significant differences in the level of education ($p=0.001$), income ($p<0.001$), marital status ($p=0.024$), underlying disease ($p<0.001$), physical activity ($p<0.001$), psychological problems ($p=0.037$), number of pregnancies ($p=0.001$) and menopause status ($p<0.001$). About 33.2% of pre-menopausal women were in cluster 1, 28% of peri-menopausal women were in cluster 3, and 55.7% of post-menopausal women were in cluster 2.

Table 4 includes the findings on differences in total menopause symptom scores, among the clusters (ANOVA test). The results show that women in cluster one had lower average symptom intensity when compared to clusters two and three, and cluster two had lower intensity than cluster three. Therefore, cluster one is made up of women who experience only mild symptoms of menopause. While cluster three has women with the most severe menopausal symptoms. There existed significant differences in total severity scores of menopause symptoms among the three clusters ($p<0.001$).

Important predictors with a significance level of 10% including age, education, income, marital status, husband's job, pregnancies, underlying diseases, psychological problems, household population, physical inactivity, and menopausal status, were included in the model. The results obtained after removing the variables backward are presented in Table 5.

Table 5 summarizes the results of the baseline category logit regression analyses, which show the significance factors of allocating in clusters 2 and 3 compared to cluster 1. Underlying disease (OR=1.50), physical inactivity (OR=1.79), more than 5 pregnancies (OR=2.11), and peri menopause (OR=1.71) were significantly increased the odds of allocating in cluster 2 relative to cluster 1. Underlying disease (OR=3.71), physical inactivity (OR=2.46), Less than sufficient income (OR=3.43), and peri menopause (OR=2.09) or post menopause

Table 1 Frequency distribution of the participants' characteristics by menopausal status

Characteristics	Menopause symptoms			Total 664	*P-value
	Pre-menopausal N(%)174(26.2)	Peri- menopausal N(%)173(26.1)	Post- menopausal N(%)317(47.7)		
Age (year) (mean ± SD)	45.89 ± 3.36	47.54 ± 3.83	54.44 ± 4.15	50.40 ± 5.5	< 0.001
Education					
Less than diploma	115(66.1)	122(70.5)	280(88.3)	517(77.9)	< 0.001
Diploma and more	59(33.9)	51(29.5)	37(11.7)	147(22.1)	
Income					
Less than sufficient	65(38.2)	81(46.8)	172(54.4)	318(47.9)	0.002
Sufficient	105(61.8)	92(53.2)	144(45.6)	342(51.5)	
Marital status					
With husband	164(94.2)	153(89.0)	259(82.2)	576(86.7)	0.001
Without husband	10(5.7)	19(11.0)	56(17.7)	85(12.8)	
Job					
Housewife	145(83.3)	154(89.0)	286(90.2)	585(88.1)	0.072
Employed	29(16.7)	19(11.0)	31(9.8)	79(11.9)	
Husband job					
Official employee	42(24.1)	52(30.1)	100(31.5)	194(29.2)	0.019
No-Official employee	95(54.6)	76(43.9)	117(36.9)	288(43.4)	
Unemployed	26(14.9)	31(17.9)	65(20.5)	122(18.4)	
N. Pregnancies					< 0.001
0–2	47(27.0)	32(18.5)	34(10.7)	113(17.0)	
3–4	111(63.8)	119(68.8)	158(49.8)	388(58.4)	
> 5	13(7.5)	22(12.7)	122(38.5)	157(23.6)	
Underlying diseases					< 0.001
Yes	61(34.7)	71(41.0)	166(52.5)	298(44.9)	
No	113(65.3)	102(59.0)	150(47.5)	365(55.0)	
Psychological problems					
Yes	24(13.8)	21(12.2)	47(14.9)	92(13.9)	0.710
No	150(86.2)	151(87.8)	268(85.1)	569(86.1)	
Household population					
< 3	26(14.9)	15(8.7)	32(10.1)	73(11.0)	0.010
4–5	111(63.8)	109(63.4)	96(30.5)	316(47.8)	
> 6	37(21.3)	48(27.9)	187(59.4)	272(41.1)	
N. Children					0.010
None	12(7.2)	8(4.7)	53(18.2)	73(11.1)	< 0.001
1–2	106(63.5)	111(65.7)	177(60.8)	394(59.3)	
≥ 3	49(29.3)	50(29.6)	61(21.0)	160(24.1)	
BMI ($\frac{kg}{m^2}$)					0.065
≤ 24.9	28(16.2)	36(20.9)	83(26.4)	147(22.1)	
> 24.9	146(83.8)	136(79.1)	231(73.6)	513(77.3)	
Physical activity					
Yes	57(32.9)	51(29.7)	102(32.4)	210(31.8)	0.771
No	116(67.1)	121(70.3)	213(67.6)	450(68.2)	

Underlying diseases: Diabetes, Heart Disease, Chronic Respiratory Diseases, Cancer, Kidney Disease and etc.

Psychological problems: Anxiety Disorders, Mood Disorders, Psychotic Disorders, Personality Disorders

N. children: Number of children living with the family at home

* P-value of chi-square statistical test

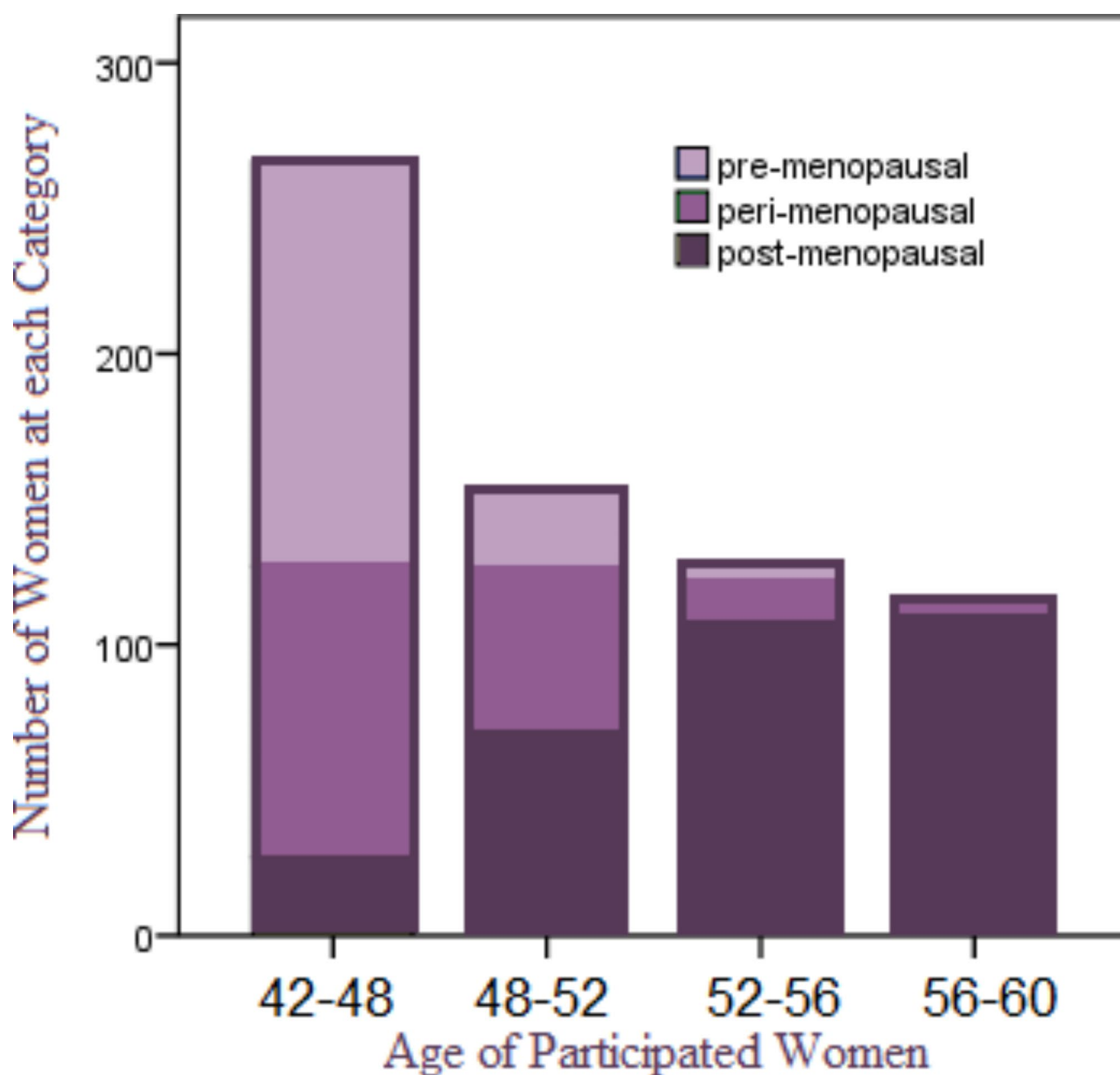


Fig. 1 Menopause stages in different age groups of women

(OR=2.02) were significantly increased the odds of allocating in cluster 3 relative to cluster1.

Discussion

This research categorized women into three groups based on the intensity of their menopausal symptoms. The mild group had the least severe symptoms, while the moderate and severe groups experienced increasingly worse symptoms. The results of baseline category logit regression analyses showed that certain factors (having an underlying disease, having more than five pregnancies, low income and not engaging in regular physical activity)

increased the odds of a woman being in the moderate or severe symptom group compared to the mild group.

During menopause and post-menopause, individuals may experience a variety of physical and psychological symptoms. Of these, vasomotor and urinary-genital complaints have garnered more attention. However, there are also non-hormonal somatic, mental, and psychological symptoms, such as headaches, insomnia, anxiety, depression, fatigue, and muscle pain [39]. The frequency and severity of these symptoms varies across different societies and may be influenced by unknown factors [11, 21, 22].

Table 2 The frequency of items related to factors of the menopausal severity symptoms by menopausal status using MSSI-38*

Menopausal symptoms	Pre-menopausal	Peri- menopausal	Post- menopausal	total	P-value
Anxiety (mean ± SD)	13.09 ± 5.26a	15.06 ± 5.71b	14.5 ± 5.55b	N(%)	*0.003
Feeling tense or nervous	87(50.0)	96(55.5)	180(56.8)	363(54.7)	**0.341
Getting easily excited (that is, agitated, excited or startled)	72(41.6)	87(50.3)	151(47.6)	310(46.8)	**0.247
Panic attacks	33(19.5)	46(27.1)	66(21.2)	145(22.3)	**0.204
Feeling tired or with lack of energy	80(46.0)	107(61.8)	188(59.5)	375(56.6)	**0.004
Irritability	32(18.6)	54(31.4)	74(23.4)	160(24.2)	**0.019
Feeling anxious or nervous	65(37.6)	77(44.5)	144(45.6)	286(43.2)	**0.215
Depression (mean ± SD)	9.00 ± 3.99a	10.29 ± 4.63b	10.40 ± 4.19b		*0.001
Crying spells	54(31.2)	62(36.0)	126(39.9)	242(36.6)	**0.162
Overall decrease in the performance capacity (for example, doing less things than you are used to do)	42(24.4)	64(37.0)	121(38.4)	227(34.4)	**0.006
Feeling depressed, down or sad	31(17.8)	41(23.8)	89(28.1)	161(24.3)	**0.040
Wanting to be alone	33(19.2)	43(25.1)	84(26.8)	160(24.4)	**0.171
Decrease in physical strength	35(20.3)	53(30.8)	108(35.0)	196(30.0)	**0.004
Vasomotor (mean ± SD)	5.86 ± 3.44a	6.86 ± 3.86b	8.21 ± 3.96c		* < 0.0001
Hot flashes	48(27.6)	69(39.9)	174(55.1)	291(43.9)	** < 0.0001
Night sweats	39(22.4)	59(34.1)	155(49.1)	253(38.2)	** < 0.0001
Excessive sweating	60(34.7)	73(42.2)	175(55.2)	308(46.5)	** < 0.0001
Pain in the head and body(mean ± SD)	5.07 ± 2.71a	5.45 ± 2.60a	5.46 ± 2.89a		*0.302
Feeling dizzy or fainting	24(14.0)	28(16.6)	56(18.1)	108(16.6)	**0.524
Sense of tension and pressure on the head or body	33(19.1)	46(26.9)	85(27.2)	164(25.0)	**0.114
Headache	41(23.6)	39(22.8)	79(25.2)	159(24.2)	**0.817
Pain in the muscles and joints(mean ± SD)	6.62 ± 3.19a	7.52 ± 3.24b	8.11 ± 3.22b		* < 0.0001
Pain in the muscles and joints	66(38.4)	83(49.4)	183(58.7)	332(50.9)	** < 0.0001
Loss of sensation on the hands or feet	48(28.4)	67(39.0)	137(43.8)	252(38.5)	**0.004
Lower back pain	66(37.9)	81(46.8)	166(52.5)	313(47.2)	**0.008
Cognitive impairment (mean ± SD)	5.22 ± 2.17a	6.03 ± 2.54b	5.91 ± 2.52b		*0.003
Difficulty in concentrating	39(22.7)	54(31.4)	95(30.6)	188(28.7)	**0.121
Loss of interest in most things	27(15.6)	47(27.2)	85(27.1)	159(24.1)	**0.010
Felling a loss or lack of memory	41(23.8)	44(25.7)	95(30.4)	180(27.4)	**0.259
Urinary-Genital symptoms (mean ± SD)	4.47 ± 1.74a	5.61 ± 2.52b	5.29 ± 2.35b		* < 0.0001
Urine leakage when laughing or coughing	26(15.0)	43(24.9)	54(17.2)	123(18.6)	**0.042
Loss of sexual interest	28(16.2)	52(30.8)	95(30.4)	175(26.8)	**0.001
Vaginal dryness (feeling of dryness, burning and problems during sexual intercourse)	8(4.6)	22(12.9)	46(14.7)	76(11.6)	**0.003

Data were analyzed as number (percent). Non-identical letters indicate significant differences between different groups according to post-hoc test ($p < 0.05$)

* P-value of ANOVA, ** P-value of chi-square statistical test

In Iran, menopause is often viewed through a cultural lens that can impact how women experience and report menopausal symptoms. Menopause is often viewed as a taboo subject, resulting in many women underreporting their symptoms [40]. Furthermore, inadequate public awareness and education about menopause contribute to misconceptions regarding its effects, while barriers to healthcare access, including cost and societal expectations, impede women's ability to report and manage their symptoms effectively [41].

In the study conducted by Ashrafi et al., night sweats, joint and muscle pain and hot flashes are the most common symptoms associated with menopause among Tehran women [20].

In Mirzaei et al. study, depression, anxiety, and stress were seen in 29%, 32.2%, and 34.8% of adult residents of Yazd Greater Area, respectively [42]. In a study conducted by Delavar, showed that, five most prevalent symptoms among women around 45–63 years old in Babol, northern Iran, were irritabilities (72.1%), joint pains (70.6%), backache (61.2%), hot flushes (49.3%) and headache (49.2%) during the previous two weeks [21].

Harvey et al. study showed that, the most prevalent symptom reported among a sample of Chinese, Malay, and Indian women was low back pain, accompanied by aching muscles and joints, with a prevalence rate of 51.4% [17].

Table 3 Differences in background characteristics of the participants among the clusters

Characteristics	Cluster1 N(%) 301(45.3)	Cluster2 N(%) 131(19.7)	Cluster3 N(%) 232(34.9)	Total	*P-value
Age (year) (mean ± SD)	49.87 ± 5.52	50.81 ± 5.63	50.89 ± 5.13	50.40 ± 5.5	0.074
Education					
Less than diploma	216(71.8)	113(86.3)	188(81.0)	517(77.9)	0.001
Diploma and more	85(28.2)	18(13.7)	44(19.0)	147(22.1)	
Income					
Less than sufficient	113(37.7)	94(71.8)	111(48.5)	318(48.2)	< 0.001
Sufficient	187(62.3)	37(28.2)	118(51.5)	342(51.8)	
Marital status					
With husband	273(91.0)	111(84.7)	192(83.5)	576(86.7)	0.024
Without husband	27(9.0)	20(15.3)	38(16.5)	85(12.8)	
Job					
Housewife	260(86.4)	121(92.4)	204(87.9)	585(88.1)	0.209
Employed	41(13.6)	10(7.6)	28(12.1)	79(11.9)	
Husband job					
Official employee	92(33.2)	32(26.9)	70(33.7)	194(32.1)	0.076
No-Official employee	167(60.3)	69(58.0)	116(55.8)	352(58.3)	
Unemployed	18(6.5)	18(15.1)	22(10.6)	58(9.6)	
N. Pregnancies					
0–2	67(22.4)	16(12.4)	30(13.0)	113(17.0)	0.001
3–4	180(60.2)	71(55.0)	137(59.6)	388(59.0)	
> 5	52(17.4)	42(32.6)	63(27.4)	157(23.9)	
Underlying disease					
Yes	108(34.3)	89(67.9)	106(45.7)	298(44.9)	< 0.001
No	197(65.7)	42(32.1)	126(54.3)	365(55.1)	
Psychological problem					
Yes	36(12.0)	27(20.9)	29(18.5)	92(13.9)	0.037
No	264(88.0)	102(79.1)	203(87.5)	569(86.1)	
Household population					
< 3	39(13.1)	13(9.9)	21(9.1)	73(11.0)	0.010
4–5	158(53.0)	52(39.7)	106(45.9)	316(47.8)	
> 6	101(33.9)	66(50.4)	105(45.3)	272(41.1)	
N. Children					
None	28(9.9)	16(13.0)	30(13.5)	74(11.8)	0.736
1–2	181(64.2)	78(63.4)	135(60.5)	394(62.7)	
≥ 3	73(25.9)	29(23.6)	58(26.0)	160(25.5)	
BMI ($\frac{kg}{m^2}$)					
≤ 24.9	65(21.7)	29(22.1)	53(23.1)	147(22.3)	0.921
> 24.9	235(78.3)	102(77.9)	176(76.9)	513(77.7)	
Physical activity					
Yes	119(39.8)	29(22.1)	62(27.0)	210(31.8)	< 0.001
No	180(60.2)	102(77.9)	168(73.0)	450(68.2)	
Menopause Status					0.001
Pre-menopausal	100(33.2)	22(16.8)	52(22.4)	174(26.2)	
Peri-menopausal	73(24.3)	36(27.5)	64(28.0)	173(26.1)	
Post- menopausal	128(42.5)	73(55.7)	116(50.0)	317(47.7)	

N. Children: Number of children living with the family at home

*P-value of chi-square statistical test

In the present study, the prevalence of complaints among menopausal women was 53.6% for muscle and joint pain, 52.1% for vasomotor symptoms, 40.1% for anxiety, 31.2% for depression, and 23.7% for difficulty

with memory and concentration, which was consistent with previous studies.

Jalili et al's study aimed to assess the relationship between physical activity and the severity of menopausal

Table 4 Menopausal symptom scores by three extracted clusters

Clusters	Menopausal Symptoms						
	Anxiety	Depression	Vasomotor	headache and body pain	Muscular pain	Difficult memory and concentration	Urinary-Genital symptoms
^a Cluster1	9.78 ± 2.25	7.01 ± 2.00	5.56 ± 3.28	4.21 ± 2.00	5.78 ± 2.55	4.38 ± 1.48	4.35 ± 1.56
^b Cluster2	15.61 ± 2.94	11.16 ± 3.24	7.40 ± 3.47	5.36 ± 2.12	8.26 ± 2.98	6.33 ± 2.07	5.45 ± 2.22
^c Cluster3	22.25 ± 3.60	14.85 ± 4.42	10.83 ± 3.60	7.97 ± 3.46	10.44 ± 2.68	7.95 ± 2.87	6.50 ± 2.96
Total	14.27 ± 5.56	10.01 ± 4.30	7.25 ± 3.93	5.35 ± 2.77	7.57 ± 3.27	5.76 ± 2.45	5.16 ± 2.29
*P-value	< 0.000	< 0.000	< 0.000	< 0.000	< 0.000	< 0.000	< 0.000

Non-Identical letters indicate significant differences between different clusters according to post-hoc test ($p < 0.05$). * P-value of ANOVA test

Table 5 Results of the baseline category logistic model fitting

Clusters	Predictors	Estimate	S.E	P-value	OR	CI. 95%
2*	Underlying disease	0.406	0.188	0.031	1.502	(1.039, 2.071)
	Physical inactivity	0.582	0.195	0.003	1.789	(1.221, 2.621)
	Number of pregnancies	0.443	0.257	0.085	1.558	(0.941, 2.579)
		0.749	0.312	0.017	2.115	(1.145, 3.302)
	Menopausal status	0.538	0.252	0.033	1.713	(1.080, 4.078)
		0.408	0.237	0.066	1.504	(0.945, 2.393)
3*	Underlying disease	1.311	0.238	< 0.000	3.711	(2.385, 6.003)
	Physical inactivity	0.899	0.260	0.001	2.457	(1.437, 4.199)
	Income	1.233	0.241	< 0.000	3.430	(2.142, 5.508)
	Menopausal status	0.741	0.339	0.029	2.099	(1.080, 4.078)
		0.705	0.350	0.044	2.023	(1.019, 4.017)

*The first category was defined as baseline

symptoms in women in Ahvaz, Iran. The study identified common prevalent complaints among those experiencing moderate, severe, and very severe menopausal symptoms, including sleep disorders, muscle pain, and hot flashes [43].

Frohlich and colleagues (2000) in a study aims to identify menstrual patterns during the first year of perimenopause, identified three clusters using cluster analysis: those who experienced more of these characteristics, those who experienced less, and those who experienced few changes [44].

In the present study, women aged 42 to 60 were classified into three groups based on their symptoms. The largest group was classified in the severe symptoms cluster, comprising 317 women (47.7%). In contrast, Eun-Ok Im's study found that the majority of women were classified in the low symptoms cluster, totaling 274 women (55%).

In this research, the chi-square test, showed the three clusters differed significantly in several factors, including education level, income, marital status, number of pregnancies, number of children living with the family at home, underlying diseases, psychological problems, household population, physical activity, and menopausal status. In contrast, Eun-Ok Im's study identified significant differences among the three clusters in terms of age, education level, income, number of children, ethnicity, BMI, self-reported health, diagnosed diseases, smoking habits, physical activity, and country of birth.

Additionally, multinomial logistic regression analyses indicated that, relative to Cluster 1, Cluster 2 was less likely to be aware of their health (adj. OR=3.55), faced challenges in affording basic necessities due to family income (adj. OR=2.97), and were more likely to be in early or late peri-menopause ([adj. OR]=2.79). Compared to Cluster 1, Cluster 3 was more likely to be post-menopausal ([adj. OR]=9.19) or in early/late perimenopause ([adj. OR]=4.35), had a higher tendency to have more than three children ([adj. OR]=3.45) or one to two children ([adj. OR]=2.86), and found it very or somewhat difficult to cover basic expenses with their current family income ([adj. OR]=2.23; [adj. OR]=1.75) [45]. The findings and clusters identified in this study were similar to those discovered in Eun-Ok Im research. In a separate study of Chinese women aged 45–60, multiple random forest regressions revealed that the out-of-bag error rate reached its minimum when the top four variables—physical activity level, menopausal status, perceived health status, and parity—formed an optimal combination. Additionally, ordinal logistic regression analysis indicated that the severity of menopausal symptoms significantly decreased with higher levels of physical activity (Moderate: OR=0.26; High: OR=0.0083). Menopausal status was positively correlated with symptom severity, with peri-menopausal women having an odds ratio (OR) of 2.65 compared to premenopausal women, and post-menopausal women having an OR of 2.45. A negative

association was observed between perceived health status and the severity of menopausal symptoms (General: OR=0.61; Satisfied: OR=0.41). Furthermore, women with two children exhibited an increased risk of experiencing more severe menopausal symptoms (OR=2.32) [46]. These findings are consistent with our study results.

In the study by Alizadeh et al., multivariate logistic regression analysis revealed that the prevalence of urinary incontinence was significantly lower among Iranian postmenopausal women who had three childbirths compared to those with fewer childbirths. This finding was not consistent with the results of our study [47]. This finding was not consistent with the results of our study.

Numerous studies have linked menopause symptoms to factors such as lower socioeconomic status, smoking, insufficient physical activity, negative mood, overall symptom reporting, and attitudes toward menopause [48–50]. The findings concerning the severity of menopausal symptoms among three groups of women showed consistency with previous studies [51]. Given that the prevalence estimates of mental health tend to be significantly higher among women who continue to reside in countries affected by ongoing conflict and there is limited understanding regarding the prevalence of anxiety disorders during the menopausal transition [52]. Further investigation is required to understand the intricate relationship between anxiety, depression, and menopausal severity symptoms.

Limitations and strengths of study

The strengths of the study included the use of the clustering method to explore subgroups of menopausal severity symptoms and the utilization of the MSSSI-38 questionnaire, which measures the frequency and severity of menopausal symptoms with more items simultaneously. However, this study had some limitations, cultural attitudes and beliefs in Iran may shape women's perceptions, experiences, and reporting of menopausal symptoms, potentially leading to an underestimation of menopausal severity symptoms. Also we did not use physical activity questionnaire to measure physical activity of participants. Baseline-category logit models can reveal relationships between variables, but caution is necessary when interpreting these models for causal inferences.

Conclusion

In this study, we find three major clusters of women according to their menopausal severity symptoms. We explore that lower socio-economic status increases the risk of falling into severe clusters. Physical activity and health promotion could decrease the risk of allocating into severe clusters.

This study would be one of the first cluster analyses on menopausal symptoms of Iranian women, but has some

limitations as discussed above. Therefore, the findings need to be confirmed through further studies to identify the causal factors contributing to menopausal symptoms. The findings on significant factors influencing menopausal severity symptoms in different clusters could provide directions for future development of preventive and/or treatment interventions for menopausal symptoms of Iranian women during menopausal transition. Health policy makers would promote of regular physical activity through community-based programs. Provide tailored educational programs for women entering menopause to manage symptoms effectively. Manage psychological support services to address mental health issues associated with menopause.

Supplementary Information

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Supplementary Material 1

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Author contributions

FH: Statistical analysis, and wrote the draft of manuscript. HE: substantial contribution in primary statistical analysis. SA: Scientific advising. AS: Conceptualized this research, supervised the statistical analysis and critically reviewed the manuscript. All authors reviewed the manuscript.

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Data availability

The data are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The ethics of this study in accordance with the Declaration of Helsinki approved by IR. MUMS.RES.1394.2 code at ethics approval board of the Research of Mashhad University of Medical Sciences. The informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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