PREDICTORS AND PROTECTORS OF PATHOLOGICAL MENOPAUSE

ABSTRACT

A prospective study of 1484 women aged 35-70 years was conducted, which were divided into 3 groups - late reproductive, perimenopausal and postmenopausal. Menopausal syndrome (MS) was detected in 1369 (93.3%) women. Every third woman in peri- and postmenopause had a moderately severe MS. The metabolic imbalance worsened more as the severity of the MS increased, rather than with increasing age. Predictors of pathological menopause are identified - these are the main components of the metabolic syndrome (diabetes mellitus, hypertension, obesity); uterine fibroids, as well as urbanization and higher education. The protective factors for the development of the MS was the absence of the fact of marriage (single), medical education and waist circumference of 80 cm or less.

Key words: late reproductive stage, perimenopause, postmenopause, menopause, menopausal syndrome, metabolic syndrome.

INTRODUCTION

The demographic situation in the world is characterized by an increase in the number of women who have reached menopause from 30% in developed countries, to 50% in developing countries [1-3]. The state of health of women, starting from late reproductive to postmenopausal age, is subject to the generally recognized mechanisms of aging, due, among other things, to increasing estrogen deficiency. The hormonal imbalance that occurs during the menopausal transition leads to the emergence of vasomotor and psycho-emotional, metabolic-endocrine symptoms with the formation in 30-85% women of menopausal syndrome (MS) [4-7], and in 13-53% of metabolic syndrome (MetS) [8-10]. Domestic researchers note that MS occurs in 20–40% of women [11, 12]. In 51% of women in the period of

menopause, there is a severe course of MS, which requires urgent medical treatment. [12]. Burdened somatic and obstetric-gynecological history, as well as a cascade of pathological conditions caused by the extinction of ovarian function, provides a high comorbidity [13]. The sociocultural, ethnic characteristics of women in the region of Central Asia, and in particular, Uzbekistan, require a comparative assessment of therapeutic and preventive measures in this period of life.

The purpose of the study was to conduct a comparative assessment of the health status of women in the late reproductive, perimenopausal and postmenopausal periods, as well as to determine factors contributing to the pathological course of menopause.

MATERIALS AND METHODS

1484 women (mainly Asian nationality 1381 - 93.1%) aged 35-70 years were examined. Depending on the age, women were divided into 3 groups: Group I, (n = 618) were women aged 35-44 who are conditionally in the late reproductive period; Group II, (n = 627) women 45-54 years old - in perimenopause and Group III, (n = 239) women 55-70 years old - in postmenopause. All women underwent general clinical examination (general examination, anthropometry, changing causal blood pressure (BP)) and special gynecological examinations. In order to detect signs of MS, and determine its severity, the Modified Menopausal Kupperman Index (MMKI) was used. 256 women were determined by the colorimetric method on the analyzer firm "Hoffman-La-Roche" determined lipid fractions of blood serum: cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), very low-density lipoprotein cholesterol (VLDL) and fasting glucose level. The atherogenic coefficient (AC) was calculated by the formula A.N. Klimov: AC=(Cholesterol-HDL)/HDL.

Statistical processing of the results was performed using the software package Statistica 6.0. The significance of differences in groups was assessed

using Student's t-test, the differences were considered significant at P≤0.05. To identify predictors and protectors of the pathological course of menopause (MS), a comparative assessment of the results of the study in women with CS and without it was carried out, the odds ratio (OR) was calculated.

RESULTS

The somatic status of women was most severely affected by goiter - in 588 (39.6%), gastritis - in 334 (22.5%), chronic kidney diseases – 313 (21.1%), anemia – 246 (16.6%), and this pathology was significantly more common in women in the late reproductive period (P≤0,05). While hypertension 272 (18.3%), depression 238 (16.0%), diseases of the respiratory system 220 (14.8%) and colitis 217 (14.6%) were more common in peri- and especially postmenopausa (P ≤0.05). The overwhelming majority of women had pregnancy and childbirth in history – 1432 (96.5%), 1046 (70.5%) had artificial abortions and 326 (22%) had miscarriages. The average number of pregnancies was 5.1±0.06, childbirth - 3.0±0.03, abortions - 2.6±0.05, miscarriages - 1.4±0.05. The ratio of birth: abortion: miscarriage averaged 2.5:2:1. Every tenth (10.8%) woman with a history of chronic salpingoophoritis suffered, uterine myoma was diagnosed in 175 (11.8%) (significantly more often in perimenopause - in 105 (16.7%)), abnormal uterine bleeding was observed in 97 (6.5%), in perimenopause - in 54 (8.6%). The average age of menopause (last menstrual period) was 46.7±0.2 years, the duration of postmenopause was 6.8±0.3 years (1-38 years). Surgical menopause was in 92 (6.2%) women, premature - in 49 (3.3%), early - in 150 (10.1%).

The clinic of the MS was observed in almost all women - 1369 (93.3%), while the 1 st grade MS was more common: in women of the 1st age group - in 426 (68.9%) (Tabl. 1). The average severity of MS in peri- and postmenopausal women was observed 1.5 times more often - in 212 (33.8%) and 83 (34.7%), respectively, compared with women aged 35-44. Severe MS was noted much less frequently in all studied groups and amounted to 1.2% - in just 18 patients. The MMKI score showed predominance of the clinic of neurovegetative (18.9 ± 0.3

points) and psycho-emotional (8.2 ± 0.2 points) disorders in perimenopausal women, while metabolic and endocrine disorders were most pronounced in postmenopausal (5.3 ± 0.2 points). The total MMKI score was most pronounced in women in the peri- (31.6 ± 0.5) and postmenopausal (31.7 ± 0.79), compared with women of the late reproductive period (P≤0.05).

We carried out a comparative analysis of the frequency of the components of the MetS depending on age (Table 2) and on the presence/absence of signs of MS (Table 3). The average waist circumference for women aged 35-44 years was 87.3±0.8 cm, whereas for women the menopausal transition and postmenopause was significantly (P<0.05) higher and amounted to 90.6±0.9 and 94.6±1.4 cm, respectively.

Table 1.

The frequency of menopausal syndrome in severity, (abs,%) and the total score MMKI, (M±δ)

	group I , n=618		group II, n=627		group III , n=239		General, n=1484	
	abs	%	abs	%	abs	%	abs	%
without MS	52	8,4±1,1	52	8,3±1,1	11	4,6±1,4	115	7,7±0,7
MS	566	91,6±1,1	575	91,7±1,1	228	95,4±1,4	1369	92,3±0,7
MS I	426	68,9±1,9	355	56,6±2,0	142	59,4±3,2	923	62,2±1,3
MS II	133	21,5±1,7	212	33,8±1,9	83	34,7±3,1	428	28,8±1,1
MS III	7	1,1±0,4	8	1,3±0,4	3	1,3±0,7	18	1,2±0,3
The total score MMKI	28,1±0,44 ** *** **** (12-73)		31,6±0,46* **** (12-70)		31,7±0,79* **** (12-65)		30,1±0,30 * ** *** (12-73)	
MODA	27		30		32		29	
MEDIANA	33		30		20		33	

*P≤0.05 compared with 1 group
** P≤0.05 compared with group 2
*** P≤0.05 compared with group 3
****P≤0.05 compared with the general group

The frequency of women with waist circumference >80 cm (criterion for women in the Asian region) was 69.7; 75.9% and significantly more frequently in postmenopausal women - 87%, respectively, in groups.

The presence of MS significantly influenced the waist circumference indicator - there was a progression of severity of abdominal obesity with increasing severity of MS. Thus, waist circumference in women with MS I and III degrees was significantly more - 91.8±1.0 and 103.8±4.5 cm compared to women without a pathological course of menopause - 86.4±2.2 cm. The frequency of abdominal obesity in women with MS was recorded significantly more often - from 75.2% with grade 1 MS to 87.5% - with severe, whereas without MS, an frequency the waist circumference of more than 80 cm was observed in 68.4%.

Table 2.

The average values of metabolic syndrome - circumference waist, blood pressure (BP) and lipid fractions in women in groups, M±δ

Indicators	group I , n=618	group II, n=627	group III , n=239
Waist circumference, sm	87,33±0,80	90,55±0,85*	94,64±1,38* **
Sistolic BP, mm Hg.	121,3±3,2	130,6±4,1	138,1±3,0*
Diastolic BP, mm Hg.	73,5±3,3	83,3±3,9*	88,6±0,9 *
n=256	n=51	n=118	n=96
Cholesterol, mmol /l	4,96±0,11	5,45±0,08*	5,48±0,08*
TG, mmol/l	1,47±0,07	1,69±0,06*	1,62±0,07
HDL , mmol /l	1,21±0,06	1,14±0,04	1,17±0,04
LDL , mmol /l	3,11±0,10	3,48±0,08*	3,51±0,09*
AC, conv. unit	3,69±0,19	4,12±0,14	4,01±0,17

Glucosa, mmol /l	4,71±0,33	5,55±0,19*	5,68±0,21*

*P≤0.05 difference significantly compared with group 1
** P≤0.05 compared with group 2

Indicators of blood pressure increased with increasing age and on average were: systolic BP - from 121.3±3.2 to 138.1±3.0 mm Hg. and diastolic BP - from 73.5±3.3 to 88.6±0.9 mm Hg. The frequency of women with BP higher than 135/85 mm Hg. also increased with increasing age - from 20.6% to a significant increase in the frequency in the postmenopausal women to 47.3%.

Comparison of BP in women with MS also showed a distinct increase depending on the severity of MS. The frequency of high BP (above 135/85 mm Hg) as the degree of severity increased, the MS increased exponentially and amounted to 21.7% with mild severity of MS, 46.5 and 77.8% with moderate and severe the severity of menopausal disorders.

In 265 women, serum lipid fractions were examined. The results showed an increase in the average levels of cholesterol (from 4.96 to 5.68 mmol / l), T (from 1.47 to 1.62 mmol / l), LDL (from 3.11 to 3.51 mmol / l), P <0.05), CA (from 3.69 to 4.1) and an unreliable decrease in the level of HDL (1.21 to 1.17 mmol / l) in the blood serum of women depending on age. Starting from the perimenopausal age, there is a clear tendency for the development of dyslipidemia and its aggravation in postmenopausal women. Analysis of the incidence of dyslipidemia showed a significant (P <0.05) increase (almost twice) in the number of women with elevated levels of LDL (41.2% in late reproductive and 71.9% in postmenopausal women) and AC (31.4 and 57.3%, respectively). The glycemic profile was represented by hyperglycemia in a small number of women (from 2 to 6.3% in groups) and impaired glucose tolerance (from 3.9 to 10.4%), while the average glycemia did not reach significant indicators - 6.1 mmol/l Another picture was noted in women with MS. Every 10th women (9.1%) with grade 2 MS had hyperglycemia, a violation of glucose tolerance was observed in every 6th (15.2%) and every 4th (23.1%) women with MS 2 and 3 degrees.

146 The MS was diagnosed based on the criteria of the International Diabetes
147 Federation (ADF), The National Cholesterol Education Program (NCEP), Adult
148 Treatment Panel III (ATP III) in a modification of 2009, taking into account
149 ethnicity [14, 15].

150 Table 3.

151 Average values of MetS in women with MS and without MS, M±δ

Indicators	MS I , n=923	MS II , n=428	MS III , n=18	General MS, n=1369	Without MS, n=115
Waist circumference, sm	88,71±0,67	91,75±1,02*	103,75±4,53***	90,0±0,56***	86,44±2,2*****
Sistolic BP, mm Hg.	128,7±1,8	136,2±3,3*	144,0±8,2	132,4±2,2	118,3±3,0 ***** *** ****
Diastolic BP, mm Hg.	78,5±3,0	92,5±1,3*	94,3±7,8*	85,2±1,9**	75,4±1,7***** ****
n=256	n=112	n=88	n=8	n=208	n=57
Cholesterol, mmol /l	5,36±0,07	5,56±0,09	6,31±0,28***	5,51±0,06****	4,68±0,08***** *****
TG, mmol/l	1,65±0,05	1,74±0,08	1,71±0,16	1,68±0,04	1,36±0,07***** *****
HDL , mmol /l	1,14±0,03	1,11±0,05	1,15±0,08	1,13±0,03	1,21±0,04
LDL , mmol /l	3,43±0,07	3,58±0,08	4,38±0,24***	3,54±0,05*****	2,81±0,08***** *****
AC, conv. unit	4,04±0,13	4,44±0,16	4,53±0,36	4,21±0,10	2,91±0,14***** *****
Glucosa,	5,59±0,08	5,52±0,09	6,1±0,26**	5,79±0,06***	4,43±0,05***** *****

mmol /l					

*P≤0.05 compared with group MS I
** P≤0.05 compared with group MS II
*** P≤0.05 compared with group MS III
****P≤0.05 compared with the General MS group

Of the examined 256 women aged 35 to 70, formed menopausal metabolic syndrome (MMS) was observed in 81 (30.6%). The most vulnerable period was the menopausal transition - MMS was diagnosed in every third woman - 40 (33.9%), whereas in women in the late reproductive period and postmenopausal women it was less common - in 14 (27.5%) and in 27 (28.1%), respectively. In the presence of the clinic of the MS, the chances of developing MMS increased almost 4 times. 74 out of 208 (35.6%) women with MS had MetS, whereas among women without manifestations of MS, it was less common 3 times less - only 7 out of 57 (12.3%). Most often, menopausal MMS was diagnosed in women with moderately severe MS - almost every second - 48 (54.5%), with MS 1 degree - in 23 (20.5%), and in MS 3 degree - in 3 (37.5%).

DISCUSSION

The analysis of the course of pre-, peri- and post-menopause showed a significant influence of social factors on the development of pathological menopause. Thus, the MS was noted significantly more often among the residents of the city - 72.0 against 54.8% without a clinic of the MS (OR = 2.1), women with higher education - 48.4 against 33% (OR = 1.9). The protective factors behind the development of a clinic at the MS are the absence of the fact of marriage (single) - 1.5 versus 5.2% (OR = 0.3) and medical education - 69.6 versus 79.1% (OR = 0.6), which is the most likely associated with access to health care and awareness. A significant factor in the development of MS with the formation of MetS is the presence in the history of somatic and gynecological diseases, such as components of MetS - diabetes - 7.4 against 0.9% (OR = 9.1), hypertension - 20.5 against 10.4% (OR = 2.2); as well as surgical menopause - 6.5 versus 0.9% (OR = 7.9), uterine mioma - 12.3 versus 3.5% (OR = 3.9), overweight and obesity - 22.2

against 26.8% (OR = 2.3). Waist circumference <80 cm is the protective factor for the development of the MS (OR = 0.5). With the progression of symptoms of the MS increases both the frequency and severity of the components of MetS, which proves the validity of the existence of the fact of MMS. The glycemic profile is exacerbated by the severity of the MS, rather than increasing age.

The most significant predictors of MS development (BMI ≥ 25 and higher), which is consistent with the literature data [16], (OR = 7.0), the presence of MetS (OR = 3.9), a high AC (OR = 6.9), due to dyslipidemia ((OR = 2.2).

CONCLUSION

The premorbid background for the development of the pathological course of menopause is a burdened somatic and obstetric-gynecological anamnesis. An earlier onset of menopause (46.7±0.2 years) in women in the region was identified, in contrast to global data (50±2 years) [17, 18]. The question of premature and early onset of menopause in almost every tenth woman in the region remains relevant. The presence of indicators of MetS significantly aggravates the course of menopause, causing a high comorbidity and the development of a MS clinic.

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