Original Article

The Higher Severity Index of Vasomotor Perimenopausal Symptoms Signals the Need to Evaluate Coexisting Metabolic Syndrome for CVD Risk Factors Stratification Experience

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ABSTRACT

Objective: To sensitize the general public and medical community about recognizing the association of severity index of perimenopausal syndrome and CHD. Components of MS are preventable through early intervention by lifestyle modification and if needed pharmacotherapy.

Study Design: Observational Cross Sectional study

Place and Duration of Study: This study was conducted at the Rai Medical College Teaching Hospital, Sargodha from June 2022 to March 2023.

Materials and Methods: All perimenopausal patients with the cardinal vasomotor symptoms, between 30-70 years were invited into this study. Recording elements of MS, basic biodata, frequency and severity of VSM perimenopausal symptoms was recorded with the help of trained paramedical staff on the prescribed modified MENQOL proforma. (1, 2 & 4) The composite score was calculated by multiplying the average weekly occurrence of symptoms with severity score for each symptom.

Results: We had 436 patients during the study period who voluntarily consented and completed the study. We had 49 known diabetics and 191 hypertensives, 30% and 69% in transition and postmenopausal phase for DM and 11%, 18% and 71% respectively for HTN. No underweight female had vasomotor symptom. We had 45 (11%) in early menopausal group, 2.22%, 22.22% and 66.67% was the distribution in different weight categories. We had 101 (24.88%) females in menopausal transition group, 12.87%, 31.68 % and 55.45%) was the distribution. We had 260 (64.15%) females in postmenopausal group, 6.92%, 11.15%, 35.77% and 46.15% was the distribution.

The females having composite severity score between 50 and 75, the distribution was 12, 26, 19 and 35. The females having composite severity score from 76-100, it was 16, 46 and 67. The females having composite severity score above 100, it was 1, 5, 70 and 104. Of the 49 (12%) diabetics, 4% scored 50-75, 26% scored from 76-100 and 69% scored above 100 on composite symptom severity score. Of the 191 hypertensives 11% scored 50-75, 71% scored from 76-100 and 52% scored above 100 on composite symptom severity score.

Conclusion: These factors of metabolic syndrome do cluster around menopause, higher the severity score the higher becomes chances of having CHD. They must be identified and proper interventions at an earlier stage have a preventive and corrective effect on future development of clinically evident CHD

Key Words: peri-menopausal syndromes, vasomotor perimenopausal symptoms, hot flushes

Citation of article: Rana MM, Nagra SR, Awan ZL, Akhtar MS, Rauf Q, Afzal MW. The Higher Severity Index of Vasomotor Perimenopausal Symptoms Signals the Need to Evaluate Coexisting Metabolic Syndrome for CVD Risk Factors Stratification Experience. Med Forum 2023;34(5):2-5.

INTRODUCTION

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Received: April, 2023
Accepted: April, 2023
Printed: May, 2023

Every female is expected to experience the physiological changes of Menopause (MNP) anywhere after the age of 30 years to around 70 due to fading female hormones and around 50-80% do experience some of these with varying severity, ranging from a mild nuisance to disabling, during perimenopausal period lasting on average 5 to 7 years or more. This set of symptoms complex is called VMS consisting of hot flushes, sweating, palpitation and extreme fluctuation in Blood Pressure (BP). They peak around forties to mid-fifties and may have a circadian rhythm, nocturnal symptoms being more disturbing. As these symptoms may start while females are still menstruating or long after cessation of periods especially after hysterectomy, many a times females fail to appreciate or recognize

them.[1] Both standard and modified self-administered versions of Menopause-Specific Quality of Life questionnaire (MENQOL) questionnaire are used to quantify the impact of different aspects of MNP.[2] Along with gestational diabetes (GDM) and gestational hypertension menopausal symptoms has been implicated along with the components of MS i.e. Diabetes Mellitus (DM), Hypertension (HTN), Obesity and Dyslipidemia for Cardiovascular Diseases (CVD) risk stratification by the American Heart Association (AHA) since 2011.[3]

A staggering 1.2 billion females are projected to be in peri- or postmenopausal phase by 2030 and 4.7 million will be added each year. Menopause was added in the list of CVD risks back in seventies. Female-specific CVD risk factors i.e. GDM and pregnancy-induced hypertension were added quiet late to the list by the American Heart Association in 2011. In terms of cardiovascular risks, menopause marks the end of protection. In post-menopausal years traditional factors of metabolic syndrome also cluster to augmentation CVD risk.[4,5]

The realization of association between PostMNP and increase in CVDs has been there in the literature, up to 80% peri-menopausal women experience VSM and the prevalence is modified by multiple factors like age, ethnicity, education, smoking, and mood, these symptoms can be used as a surrogate markers for CHD. Generally women have a higher prevalence MetS after menopause. Recent data indicate that CHD risk may increase more rapidly before menopause rather than after menopause.[6]

Inclusion Criteria: Any female presenting with symptoms suggestive of perimenopausal syndrome between 30-75 years. Patients not menstruating due to surgical hysterectomy but still having vasomotor symptoms were included. STRAW staging system was used to define the different stages of pre menopause (Pre MNP) menopause (MNP) and Postmenopausal (Post-MNP) period.[1]

Exclusion Criteria: Pre-menopause, Medical and Iatrogenic conditions that can masquerade as Hot Flushes like Anxiety disorders, Autoimmune disorders, Carcinoid syndromes, Diabetic autonomic dysfunction/hypoglycemia, Epilepsy, any Infection or febrile illness, Insulinoma/pancreatic tumors, Leukemia/lymphoma, cancer survivors, mast-cell disorders, New-onset hypertension, Thyroid disease, Tuberculosis, Use of selective-reuptake inhibitors or serotonin norepinephrine-reuptake inhibitors.

Hormonal (HRT) or non-hormonal replacement (Tibolol) therapy.[3]

MATERIALS AND METHODS

This study was conducted on the females presenting to OPD with the cardinal vasomotor symptoms, fluctuating BP, hot flushes, palpitation and sweating, between 30-70 years. After securing informed consent, applying inclusion and exclusion criteria and recording elements of MS i.e. DM, HTN, Obesity and Dyslipidemia, basic bio data, frequency and severity of VSM perimenopausal symptoms was recorded with the help of trained paramedical staff on the prescribed proforma. (1, 2&4) Modified version of MENQOL questionnaire (1996) was applied. This questionnaire divide menopausal symptoms consisting of 29 items divided into four domains: vasomotor (3), psychosocial (7), physical (16) and sexual (3). We explored only vasomotor domain, hot flashes, sweating, palpitation and hypertension. Each item has a severity score ranging from 0 (not at all bothered) to 6 (extremely bothered). All items follow the same format in which the woman is asked whether she has experienced the item in the previous month. Then she is asked to give an average frequency of each selected item in last one week and to assign bothersomeness. The composite score is calculated by multiplying the average weekly occurrence of symptoms with severity score for each symptom.[2] If the composite score is above 50% of the total or if the patient has other factors of MS early intervention will be recommended by physician or in consultation with cardiologist and/or gynecologist.

Sample size and sampling technique: A minimum sample size of 398 was calculated to maintain a 5 percent margin of error, a 95 percent confidence interval and a 75 percent response distribution, using WHO sample size calculator.

Statistical Analysis: Data analysis was conducted using Statistical Package for Social Sciences software version 25. Descriptive statistics (i.e. frequency distribution, percentages, mean and standard deviations) will be the primary analytical methods.

RESULTS

We had 436 patients during the study period who voluntarily consented and completed the study.

Table No.1: Diabetese Mellitus (DM) and Hypertension (HTN) Composite Symptom Severity Score Above 50. (N 406)

	DM N = 49 (12.06%)	**HTN N = 191 (47.04%)**
Early Menopase	0 (0.00%)	21 (10.99%)
Menopause Transition	15 (30.62%)	35 (18.32%)
Postmenopause	34 (69.38%)	136(71.20%)

11% were early menopausal (mean age 42+0.59), 25% were in transitional phase (mean age 48+0.64) and 64% were in post-menopausal phase (mean age 54+0.35). Only 7% had composite score < 50, these were excluded leaving 406 females in the final analysis.

We had 49 known diabetics, 15 (30%) were in menopausal transition and 34 (69%) were in postmenopausal phase. We had 191 known hypertensive patients, 21 (11%) were early menopausal, 35 (18%) were in menopausal transition and 136 (71%) were in postmenopausal phase.

No underweight female had vasomotor symptom. We had 45 (11%) in early menopausal group, 1 (2.22%) was overweight, 10 (22.22%) were obese and 30 (66.67%) were extremely obese. We had 101 (24.88%) females in menopausal transition group, 13 (12.87%) were overweight, 32 (31.68 %) were obese and 56 (55.45%) were extremely obese. We had 260 (64.15%) females in postmenopausal group, 18 (6.92%) females had normal weight, 29 (11.15%) were overweight, 93 (35.77%) were obese and 120 (46.15%) were extremely obese as defined by BMI.

Table No.2: Obesity and Composite Symptom Severity Score Above 50. (N 406)

No.		Early Menopausel N = 45 (11.08%)	Menopausal Transition N = 101 (24.88%)	Post Menopausal N = 260 (64.04%)
1	BMI. Undewight	0 (0.00%)	0 (0.00%)	0 (0.00%)
2	BMI. Normal Weight	0 (0.00%)	0 (0.00%)	18 (6.92%)
3	BMI. Overwieght	5 (11.11%)	13 (12.87%)	29 (11.15%)
4	BMI. Obese	10 (22.22%)	32 (31.68%)	93 (35.77%)
5	BMI. Extreme Obesity	30 (66.67%)	56 (55.45%)	120 (46.15%)

Table No.3: Composite Symptom Severity Score Above 50, Obesity, DM, HTN. (N 406)

	Normal BMI N = 18 (4.43%)	Overweight BMI N = 47 (11.58%)	Obese BMI N = 135 (33.25%)	Extremely Obese BMI N = 206 (50.74%)	DM N = 49 (12.06%)	HTN N = 191 (47.04%)
Score:50-75	12 (66.67%)	26 (55.32%)	19 (14.07%)	35 (16.99%)	2 (4.08%)	21(10.99%)
Score:76-100	5 (27.78%)	16 (34.04%)	46 (34.07%)	67 (32.52%)	13 (26.53%)	71(37.18%)
Score:>100	1 (5.55%)	5 (10.64%)	70 (51.86%)	104 (50.49%)	34 (69.39%)	99(51.83%)

The females having composite severity score between 50 and 75, 12 had normal BMI, 26 were overweight, 19 were obese and 35 were extremely obese. The females having composite severity score from 76-100, 5 had normal BMI, 16 were overweight, 46 were obese and 67 were extremely obese. The females having composite severity score above 100, only 1 had normal BMI, 5 were overweight, 70 were obese and 104 were extremely obese. Of the 49 (12%) diabetics, 4% scored 50-75, 26% scored from 76-100 and 69% scored above 100 on composite symptom severity score. Of the 191 hypertensives 11% scored 50-75, 71% scored from 76-100 and 52% scored above 100 on composite symptom severity score.

DISCUSSION

Women are disproportionately affected by traditional risk factors for CVD especially midlife due to hormonal changes along with social, environmental, and economic factors leading to the clustering of components of metabolic syndrome. United Kingdom (UK) population-based Million Women Study showed that both early and late menarche pose an increased risk of CHD in later life. Polycystic ovaries and associated hyperinsulinemia affecting between 5% and 10% of women worldwide increases risk for CVD by 4 fold as reported by The Coronary Artery Risk Development in Young Adults (CARDIA) study. More frequent flares heralds a worse CV prognosis.[7] Female-specific biological factors like Gestational DM and HTN, pre-eclempsia and eclempsia and other adverse pregnancy outcomes have lasting implications for long-term CV risk and mortality.[8,9]

In this study the incidence of existing DM and HTN rose from 30% to 34% for DM and from 10% to 71% for HTN, it was expected to increase with passing years. The number of patients with obesity and extreme obesity increased with passing years proving the clustering of risk factors theory. The most significant trend is reflected in table 3, the severity index shows a sharp upward trend with rising BMI values in all three phase of menopause and in all three categories of increasing severity index.

CHD related mortality for diabetic women is estimated 2.1 million (1.81-fold) versus 1.8 million (1.48-fold) in diabetic men, risk of heart failure is 5-fold higher in diabetic women as compared with non-diabetic women. Women have higher rates of coronary microvascular dysfunction (CMD). Women with HTN have a relatively higher population-adjusted CV mortality in menopausal years.[10,11] The Framingham Heart Study showed that obesity on its own, older females have 64% increased CHD risk compared with 46% in men.[12]

Ovarian aging does have important role, lipids become more atherogenic and total fat is shifted to more of visceral variety, impairing glucose metabolism and blood pressure.[13,14]

Clinically significant coronary ischemia in spite of no obstructive coronary artery disease (INOCA) caused by CMD is now being increasingly recognized and diagnosed in women. CMD must be entertained in the workup to explain evidence of coronary ischemic events without evidence of obstructive CHD on

angiography, it may be present in 2/3rd of women having no evidence of significant obstruction (defined as < 50% stenosis on diagnostic angiography).[15]

Earlier surgical menopause (e.g. <45 years) is associated with over 20% higher risk of CVD. The North American Menopause Society Hormone Therapy Position Statement Advisory Panel, 2017, does recommend a 'timing' hypothesis, HRT after a surgical menopause before 45 lowers the risk of CHD until at least the median age of menopause (i.e. 50–52 years.[16]

Role of estrogen during transition and after MNP is less clear, new evidence suggest follicle stimulating hormone as a proxy measure of the menopause transition, and CVD risk preferably with multiple reading over time.[17]

CONCLUSION

When DM and Hypertension are already present in a female approaching menopause, the increased risk of CHD in these patients has been documented. Obesity and the degree of obesity reflecting in increasing BMI have a linear relationship with the severity score, the higher in itself shall be taken as surrogate CHD risk due to the strength of relationship. These factors of metabolic syndrome do cluster around menopause, higher the severity score the higher becomes chances of having CHD. They must be identified and proper interventions at an earlier stage have a preventive and corrective effect on future development of clinically evident CHD.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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