

Association of Vaginal Maturation Index and Vaginal pH with the Most Bothersome Symptoms of Genitourinary Syndrome of Menopause

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ABSTRACT

Introduction: Genitourinary syndrome of menopause (GSM) is a term used to characterize the symptoms and manifestations of estrogen deficiency in the female genitourinary tract. This syndrome has commonly occurred in postmenopause women yet often undertreatment due to lack of awareness either by physician or the patient herself.

Aims and objectives: To assess the association between vaginal maturation index (VMI) and vaginal pH with the most bothersome symptoms of GSM.

Methods: This was a cross-sectional study carried out from August to December 2020 in Medan, Sumatera Utara, Indonesia. A total of 150 postmenopause women who meet the criteria were recruited. This study data consisted of primary data of characteristic background, estradiol level, score of VMI, and vaginal pH. The subjects were divided into two groups regarding the existence of GSM related symptoms. The symptomatic women were asked for the most bothersome symptoms and analyzed based on its severity.

Result: The majority of menopausal women (70.7%) did not report any GSM-related symptom. The most bothersome symptom (MBS) for this study is vaginal dryness and dyspareunia. The women with mild symptoms showed statistically higher vaginal pH and lower VMI compared to the subjects with moderate/severe symptoms ($p < 0.05$).

Conclusion: Lower VMI and higher vaginal pH associated with the severity of GSM symptoms.

Keywords: Genitourinary syndrome of menopause, Menopause, Vaginal cytology, Vaginal maturation index.

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INTRODUCTION

The menopause is a universal condition marked by the absence of menstruation for an extended period of time, indicating the change of a woman's life from a reproductive to a nonreproductive state. In the past two decades, researchers have made remarkable achievements in their perception of menopausal biological alterations and their association with menopausal symptoms. Urogenital symptoms tend to be the most common problem in the late stages of menopause, since they seem to get worse over time.¹

Genitourinary syndrome of menopause (GSM) is a recent terminology coined by The International Society for the Study of Women's Sexual Health (ISSWSH) and The North American Menopause Society (NAMS) to define the symptoms and signs of estrogen deficiency on the female genital and urinary tract of menopausal women. Vaginal dryness, burning, and irritation; urinary symptoms and conditions of dysuria, urgency, and recurrent urinary tract infections; and sexual symptoms of pain and dryness are all signs of this syndrome.²

GSM symptoms are very frequent, affecting roughly one-quarter to more than three-quarters of postmenopausal women.³ Unlike vasomotor symptoms, which also intensify over time, GSM tends to worsen without treatment. Menopause's genitourinary syndrome has a major negative impact on a woman's reproductive wellbeing and quality of life.⁴ Reduced estrogen and progesterone receptors in the urogenital tract cause this syndrome. A lack of estradiol causes a variety of hormonal changes in the vaginal tract, including a loss of elasticity, which causes shortening and shrinking, and the loss of

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the vaginal rugae.⁵ There is a reduction in epithelial layer, vaginal secretion, musculature and vascularity thus led to GSM.^{2,4,5}

After all disorders have been ruled out, GSM will be diagnosed based on signs and physical findings.² Recently, there is still no agreement on GSM's objective and measurable marker. Evaluating a vaginal maturation index (VMI) and measuring the vaginal pH are considered simple, useful, and inexpensive tool for diagnosis GSM.⁶ The most bothersome symptom (MBS) method is also useful for diagnosing and assessing treatment response.⁷ Currently, the most reliable method of diagnosing GSM is to integrate the MBS approach with a physical examination.^{2,3}

Regarding the importance of diagnosis and screening for GSM, we studied the association between VMI and vaginal pH with the symptoms of GSM which assessed by self-reported MBS approach.

MATERIALS AND METHODS

This was a cross-sectional study carried out from August to December 2020 in Medan, Sumatera Utara, Indonesia. A total of 150 women were recruited. The inclusion criteria for this study were women whom had not been having menstrual bleeding minimal 12 months and aged less than 75 years old. The exclusion criteria were had history of oophorectomy, chemotherapy, active smoker, using hormonal replacement therapy and suffering chronic disease. All women were informed about the study protocol and required to provide written consent. Detailed history and examination of all patients were taken for the study variables including age, onset of menopause, parity, sexual activity, body mass index, blood pressure, and estradiol level.

GSM manifestations such as vaginal dryness, discomfort, burning, dysuria, and dyspareunia were asked to the subjects. A self-assessment questionnaire of GSM symptoms was administered by subjects who had one or more of the symptoms, and it consisted of questions about the severity of one of five individual GSM symptoms. Each woman was asked to describe the GSM symptom which had the greatest influence on her quality of life, if any, she will be instructed to rate it as the MBS.

All the subjects were undergone sterile speculum examination. Vaginal pH level was measured by pH indicator paper with color scale which range from pH 2 to 10.5. The paper was contacted to right lateral mid third vagina for 5 seconds and the color is compared with color scale and thus pH value is determined. Cytological evaluation for VMI was performed by vaginal smear collected

from left lateral wall of mid third of vagina and mounted on a slide. Smear is immediately fixed in an alcohol 96% ether dip for 1 hour and then stained with Papanicolaou stain. Each slide is evaluated in department of Pathology Anatomy, Faculty of Medicine, Universitas Sumatera Utara, Medan. In a total of 100 exfoliated vaginal cells, parabasal cells, intermediate cells, and superficial cells were count and results were expressed as the maturation value. Parabasal cells are small rounded cells with large nuclei comprising 50–70% of the total cell size. Intermediate cells have small nuclei with round cell. Superficial cells have smaller nuclei, rectangular cell membrane with abundant cytoplasm with nucleus comprising 10–20% of the cell. Superficial cells, intermediate cells, and parabasal cells were assigned a point value of 1, 0.6, and 0.2, respectively. The number of cells in each category will be multiplied by point values and all three results will be added to the total score of VMI.

The data were analyzed using Statistical Package for the Social Science program (SPSS Inc., Chicago, Illinois, USA) 24th version. Data entered as numerical or categorical, as appropriate. Quantitative and qualitative data were shown as mean ± SD or median (min–max) and as frequency (percentage), respectively. Statistical analysis was done using Chi-square test for qualitative data and two-sample *t* test for quantitative data used if it is normally distributed and Mann-Whitney is used if it was not normally distributed; *p* <0.05 was considered to be of statistical significance.

RESULTS

Characteristics of subjects based on age, duration of menopause, parity, sexual activity, body mass index, blood pressure, and levels of estradiol, vaginal pH, and VMI are described in Table 1.

Table 1: Characteristics of subjects based on GSM

Variables	Menopausal women (n = 150)		p value
	GSM (+) n = 44 (29.3%)	GSM (-) n = 106 (70.7%)	
Age (years old)	58.12 ± 5.2	56.19 ± 5.12	*0.207
Duration of menopause (years)	5 ± 3.5	3 ± 3.1	*0.042
Parity			†0.396
Nullipara	5 (11.3%)	12 (11.3%)	
Secundipara	11 (25%)	31 (29.2%)	
Mutipara	28 (77.7%)	63 (65.5%)	
Sexual active			†0.041
Yes	30 (68.2%)	88 (83%)	
No	14 (31.8%)	18 (17%)	
Body mass index (kg/m ²)	23.88 ± 3.82	23.62 ± 3.25	*0.344
Blood pressure			
Systolic (mm Hg)	126.2 ± 19.5	128 ± 18.6	*0.212
Diastolic (mm Hg)	78.8 ± 12.3	79.9 ± 11.9	*0.321
Estradiol (pg/mL)	11.9 (11.7–108.4)	13.2 (11.8–151.5)	‡0.025
Vaginal pH	5.9 ± 0.52	5.1 ± 0.22	*0.014
VMI			* <0.001
Parabasal cells	2.31 ± 3.2	1.15 ± 0.82	
Intermediate cells	78.8 ± 15.9	30.55 ± 21.78	
Superficial cells	17.55 ± 18.9	68.35 ± 22.9	
Score	51.86 ± 11.5	62.22 ± 12.1	

GSM, genitourinary syndrome of menopause; VMI, vaginal maturation index; * *t* independent; † Chi-square; ‡ Mann-Whitney

The subjects were divided into two groups according to the present of GSM-related symptoms. The majority of menopausal women were participated in this study (70.7%) did not report any GSM-related symptoms. There were no differences in both group regarding the age duration of menopause, parity, sexual activity, body mass index, and blood pressure. Subjects in GSM (+)-related symptoms showed a statistically lesser estradiol level, higher vaginal pH, and lower total VMI score compared to the subjects in GSM (-)-related symptoms ($p = 0.025$; $p = 0.014$; $p \leq 0.001$, respectively).

The distribution of symptoms was described in Table 2. The severity of symptoms which are experienced by the patient was classified as mild, moderate, and severe. The severity was completed by the patient subjectively. From 44 patients with GSM (+)-related symptoms report vaginal dryness and dyspareunia as the most bothersome symptoms ($n = 20$, $n = 16$, respectively).

We analyzed the association of vaginal cytology consisting vaginal pH and VMI with two most reported MBS, vaginal dryness and dyspareunia from the subjects of this study. The severity of MBS was divided into mild and moderate/severe. From Table 3 we showed two analyses. In MBS-vaginal dryness analysis, the subjects with mild symptoms showed a statistically higher vaginal pH and lower VMI compared to the subjects with moderate/severe symptoms ($p = 0.014$; $p \leq 0.001$, respectively). A similar result has been shown in MBS-dyspareunia analysis; the subjects with mild symptoms showed statistically higher vaginal pH and lower VMI compared to the subjects with moderate/severe symptoms ($p = 0.015$; $p \leq 0.001$, respectively).

Table 2: Baseline frequency distribution of symptoms GSM and the most bothersome symptoms (MBS)

Symptoms	GSM-related symptoms (n = 44)			
	MBS	Severity		
		Mild	Moderate	Severe
Dryness	20	12	6	2
Dyspareunia	16	8	7	1
Itching	5	1	3	1
Vaginal discharge	2	1	1	0
Difficulty during urination	1	0	1	0

GSM, genitourinary syndrome of menopause; MBS, the most bothersome symptoms

DISCUSSION

In this study we found almost three quarters of subject-reported GSM-related symptoms. The mean age was no different between two groups, but GSM (+) group has longer onset of menopause compared to GSM (-) group. In the previous study Palma et al. reported that mostly GSM was identified in women 6 years after onset of menopause.³ The GSM most commonly develops related to estrogen deficiency which occurred in natural menopause.⁸

The women with symptoms were found to have lower estradiol level compared to without symptoms. Estrogen is a major factor in regulation of vaginal and lower urinary tract physiology. Both premenopausal and postmenopausal women have estrogen receptor alpha in their vaginal tissues, while estrogen receptor beta is absent or only slightly present in postmenopausal vaginal tissue.⁹ After menopause, low amounts of circulating estrogen cause physiologic, biologic, and clinical modifications in the urogenital tissues, including decreased vaginal blood flow, decreased lubrication, decreased vaginal vault versatility and elasticity, and increased vaginal pH.¹⁰

The existence of both examination findings and symptoms specific to menopause is essential for the diagnosis of GSM. Vaginal dryness, dyspareunia, discomfort or a burning sensation in the vulva, vaginal itching, dysuria, and vaginal discharge are the most commonly reported symptoms. Symptoms have a negative impact on sexual function as well as quality of life.¹¹ In this study vaginal dryness was majority picked up as MBS by the symptomatic group secondary to dyspareunia. In a study conducted in the United States, Simon et al. found that the most bothersome symptoms were vaginal dryness and discomfort during intercourse, which were identified by half of the symptomatic women.¹²

The vaginal epithelium's altering physiology following menopause is not fully understood. Reduced estrogen levels after menopause have been linked to a reduction in vaginal and cervical paracellular permeability, which may lead to vaginal dryness.¹³ The vagina has the greatest density of estrogen receptors, which decreases as the pass from the outer genitalia to the skin. Estrogen receptors have already been identified in the vaginal and vulval autonomic and sensory nerves. In hypoestrogenic state vaginal secretion is decreased and the density of sensory nociceptor neuron is increased, this condition may led to dyspareunia.¹⁴

In this study was found that vaginal pH is higher and VMI was lower in GSM (+), and regarding severity both parameters were found statistically difference between mild and moderate/severe

Table 3: Relationship of the most bothersome symptoms (MBS) with vaginal cytology

Vaginal cytology	MBS					
	Vaginal dryness (n = 20)			Dyspareunia (n = 16)		
	Mild (n = 12)	Moderate/severe (n = 8)	* p value	Mild (n = 8)	Moderate/severe (n = 8)	* p value
Vaginal pH	5.5 ± 0.32	6.2 ± 0.21	0.014	5.6 ± 0.29	6.3 ± 0.17	0.015
VMI			<0.001			<0.001
Parabasal cells	7.25 ± 4.8	12.11 ± 5.1		6.96 ± 4.6	11.15 ± 5.2	
Intermediate cells	77.3 ± 15.5	78.7 ± 14.9		77.6 ± 14.9	80.5 ± 13.4	
Superficial cells	15.55 ± 4.3	8.23 ± 3.9		17.35 ± 4.2	9.69 ± 3.8	
Score	52.02 ± 9.2	49.87 ± 8.8		53.52 ± 8.9	49.92 ± 8.9	

MBS, the most bothersome symptoms; GSM, genitourinary syndrome of menopause; VMI, vaginal maturation index; *t independent

group. Wet-mount microscopy demonstrates more than one white blood cell per epithelial cell and immature vaginal epithelial cells with comparatively large nuclei (parabasal cells) in vaginal atrophy triggered by estrogen deficiency. Cytology shows an increase in parabasal and intermediate cells, and superficial cells decrease or are absent led to lower score of VMI.¹⁵ Due to reduced glycogen content, women after menopause are less likely to have a *Lactobacillus* vaginal bacterial population and a low vaginal pH. The pH of the vaginal fluid is usual due to reduced glycogen content. Vaginal pH values above 5 are usually associated with the presence of GSM in postmenopausal women.¹⁶

In diagnosis of GSM, VMI and vaginal pH are not essential, yet this examination is routinely assessed in clinical trial.^{2,6} Through this study we recommend routine use of VMI and vaginal pH as objective sign of women urogenital health especially for women with symptoms-related GSM.

CONCLUSION

In this study we concluded that low VMI and alkaline vaginal pH were associated with the presence of GSM-related symptoms among menopausal women. Lower VMI and higher vaginal pH are associated with the severity of symptoms.

ETHICAL CONSIDERATION

The study protocol has been approved by Committee of Ethics, Universitas Sumatera Utara, Medan, Indonesia (NO:403/KEP/USU/2020). All study procedures in accordance with Helsinki's declaration of human rights.

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