Section: Obstetrics & Gynaecology

Research

VAGINAL pH VS SERUM FOLLICLE STIMULATING HORMONE LEVELS AS A MARKER OF MENOPAUSE

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Abstract

Background: The diagnosis of Menopause is usually retrospective and can be confirmed by Serum Follicle stimulating levels (FSH) > 40IU/L. Vaginal pH is an alternative test for the same. The Objectives is to determine whether vaginal pH can replace Serum FSH levels as a marker of menopause. **Materials and Methods:** This prospective cross-sectional study was conducted in the department of Obstetrics and Gynecology, Govt. Medical College, Jammu over a period of 1 year from January 2020 to December 2020. 200 females aged 45-65 years attending the OPD with menopausal symptoms were selected randomly. Vaginal pH was measured using pH micro-meter strips and serum FSH levels were measured using immunoassay methods. Data was analyzed statistically by SPSS version 21.0 of Windows. **Result:** Out of 200 subjects, 78% were postmenopausal. Mean age at menopause was 48.48± 2.29. In our study, 87.5% of the population had S.FSH ≥ 40 IU/L with the mean of 56.24± 14.65. 90% had vaginal pH ≥ 4.5 with the mean of 5.514± 1.038. Based on the study findings vaginal pH ≥ 4.5 had a sensitivity of 96.11% vs 95.36% of S.FSH. Out of 200 subjects, 180 had FSH ≥ 40IU/L and among them 173 had pH ≥ 4.5, both the variables being positively associated with menopause (p< 0.001). **Conclusion:** Vaginal pH is a simple, accurate, non -invasive and cost-effective office tool that can be used as an alternative to serum FSH for diagnosis of menopause.

INTRODUCTION

Menopause is derived from the Greek word 'men' means month and 'pausis' means cessation.[1] Menopause is a natural phenomenon signaling the reduction of ovarian function and onset of last menstrual period and is generally diagnosed in retrospective since confirmation occurs after 12 months of cessation menstrual periods. Perimenopause is defined as the transition prior to the last menstrual cycle, when a women may experience variable or irregular menstrual cycles and hormonal fluctuations, and 12 months after the final menstrual period. Perimenopause is the stage after menarche but before entering menopausal stages with normal fertility function during this phase.[2] Postmenopause is defined as the stage beginning 12 months after the last menstrual cycle.[3] In a study conducted by "National Health Centre", it was seen that the average age of menopause among Iranian women was 49.6 years, while in U.S. women, it was 51±1 years.[4] The average age of menopause in Indian women is 46.8 years.[5]

The Menopause transition is experienced by 1.5 million women each year and often involves troublesome symptoms, including vasomotor symptoms, vaginal dryness, decreased libido, insomnia, fatigue and joint pain.[6] Owing to lack of estrogen more than 80% of women experience decrease physical and mental wellbeing in the year approaching menopause.[7] It is well documented that menopausal symptoms experienced by women affect their quality of life.[8] Unfortunately, majority of the women are not aware of the changes brought about by menopause.[9] Soon after menopause there are no ovarian follicles, 1-3years after menopause, the FSH and LH levels increase, and during the next 1-3 years they reaches to a maximum level. The FSH levels are more than LH, as LH can be quickly

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cleared from the blood. Changes in circulating testosterone, and to lessser extent, estradiol level are correlated to changes in dehydroepiandrosterones in the perimenopausal transition period. Clinicians commonly identify perimenopausal women by their age, menstrual history, symptoms, and by their hormonal levels to confirm the diagnosis. The hypoestrogenic state of menopause is the cause of vaginal atrophy, vaginitis, urinary tract infections, and dyspareunia. An increase FSH level is the cause of vasoactive phenomenon such as hot flushes and sweats.[10] It is of note that increase in serum FSH, with or without a decrease of estradiol, have been shown in women over the age of 40 years yet who continue to cycle regularly.[11] Moreover abrupt fluctuations in serum FSH and estradiol may also be observed with menopausal levels returning to the normal reproductive range.[12] The diagnosis of menopause is confirmed by FSH levels more than 40 IU /L.[13] Some studies have proposed vaginal pH as another method for diagnosis of menopause. It has been known for decades that without vaginal infections, vaginal pH is ≤4.5 during reproductive years and more than 4.5 before menarche and after menopause. Contamination with cervical mucus, blood or semen leads to incorrect vaginal pH interpretation.[14] The normal vaginal pH of reproductive aged women is 3.9-4.5. During premenopausal years, vaginal pH ranges between 4.5 and 6, where lack of estrogen after menopause is associated with alkalization to about 6.5 to 7.[15] During menopause, two factors influence vaginal pH - menopausal status and the presence of potentially pathogenic organisms. In normal fertile women, lactobacilli maintain the normal acidic vaginal pH that protects the vagina against colonization.[16] At menopause, there is thinning of the vaginal epithelium, resulting in less exfoliation of epithelial cells, so lesser glycogen, and increase in the vaginal pH. Some strains of lactobacilli produce hydrogen peroxide that prevent vaginal colonization with uropathogens.[17] Therefore, exclusion of vaginitis is essential for the vaginal pH to reflect the state of menopausal vagina. There is a relationship between sufficient vaginal estrogen and the vaginal micro-organism and their metabolic products.[18] Menopause can be diagnosed by elevated serum FSH level, even before the onset of symptoms. However, this is an expensive test and according to the patient's socio-economic status, it is reasonable to choose a more cost effective, simple and non - invasive method. Some authors have suggested the evaluation of proposed vaginal pH as a good and inexpensive method. They reported that with vaginal pH more than 4.5, serum estradiol is more likely to be the same as menopausal level. Furthermore in the absence of vaginitis, a vaginal pH of 6-7.5 strongly suggest menopause.[19]

Vaginal pH can facilitate immediate, in office evaluation of age-related hormonal changes of menopause and hence can be suggested as a simple accurate and cost-effective alternative to serum FSH level in diagnosing menopause.

The purpose of this study is to determine whether vaginal pH can replace serum FSH as initial screening test for menopause.

MATERIALS AND METHODS

This prospective cross-sectional study was conducted in the department of Obstetrics and Gynecology, Govt. Medical College, Jammu over a period of 1 year from January 2020 to December 2020. 200 females aged 45-65 years attending the OPD with menopausal symptoms were selected randomly. A complete menstrual, sexual, medical and family history of menopause was obtained. A questionnaire was completed for each women including demographic characteristics (age, parity and body mass index), other gynecological disorders and clinical manifestations of menopause including vasomotor complaints, urogenital complaints and psychosocial factors.

Inclusion Criteria

Women aged 45-65 years with menopausal symptoms.

Exclusion Criteria

1. Hormone replacement therapy
2. Sexual intercourse within previous 3 days.
3. Vaginitis based on history, vaginal examination and culture in suspected cases.
4. Vaginal medications, douches

Vaginal pH was measured using pH micro-meter strips. After insertion of a non-lubricated sterile vaginal speculum, the pH strip was applied directly to the lateral vaginal wall at the outer third of the vagina until it becomes wet. Colour change of the strip was immediately compared with colorimetric scale and the measurement recorded. Care was taken to avoid cervical mucus, blood, or other substances as lubricating jelly, known to affect vaginal pH.

Blood sample was obtained by venipuncture and assayed for serum FSH levels. Serum FSH levels were measured using immunoassay methods.

Data was analyzed statistically by SPSS version 21.0 of Windows. Data was analyzed statistically by SPSS version 21.0 of Windows.

RESULTS

In our study, 200 females were taken. Their age ranged between 40 to 65 years with the mean age to be 51.59±5.648, with the maximum number of subjects to be between 46-50 years.

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Table 1:

Age in years	No.of subjects	Percentage (%)
40-45	24	12
46-50	94	47
51-55	31	15.5
56-60	33	16.5
61-65	18	9
Total	200	100

Mean age = 51.59±5.648

Table 2: Distribution of patients according to postmenopausal status.

Postmenopausal	Number of subjects	Percent
No	44	22
Yes	156	78
Total	200	100

Out of 200,156 (78%) subjects were postmenopausal.
None of the patients had history of any pelvic surgery, pelvic radiation or hormonal intake.

Table 3: - Distribution of subjects according to their serum FSH values.

FSH (IU/L)	Number of subjects	Percentage(%)
<40	25	12.5
≥40	175	87.5
Total	200	100

Mean FSH ±SD=56.248±14.65

In our study,175 (87.5%) out of 200 subjects had serum FSH to be greater than equal to 40IU/L ranging from 25.0 to 89.8 with a mean of 56.24±14.65.

Table 4: Distribution of subjects according to their vaginal pH.

pH	Number of subjects	Percentage
<4.5	20	10
≥4.5	180	90
Total	200	100

Mean pH ± SD =5.514± 1.0382

Out of 200, 180(90%) of the subjects had pH ≥4.5, ranging from 3.0 to 7.8 and a mean of 5.514±1.0382.

Table 5: Distribution of subjects according to the age at menopause.

Age at menopause	Number of subjects	Percentage
<46	10	6.4
46 to<48	54	34.6
48 to <50	42	26.9
50 to <52	33	21.2
52 to < 54	14	9
≥54	3	1.9
Total	156	100

Mean age at menopause ±SD= 48.48±2.29.

In our study, 156 subjects were postmenopausal. The mean age at menopause was 48.48±2.29 years.

Table 6: Vaginal pH as a predictor for menopause.

pH value	Post-Menopausal	Premenopausal	Total
≥4.5	150	24	174
<4.5	6	20	26
Total	156	44	200

In our study it was observed that out of 200 patients,150 postmenopausal females had pH ≥4.5 and 6 had pH < 4.5 and out of 44 premenopausal females 24 had pH ≥4.5 and 20 with<4.5.
As calculated pH value >4.5 in detecting postmenopausal status of the female had a sensitivity of 96.11% and specificity of 45.45%.

Table 7: FSH as a predictor for menopause.

Serum FSH	Postmenopausal	Premenopausal	Total
≥40	149	20	169
<40	7	24	31
Total	156	44	200

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Out of 156, Post-menopausal females 149 had FSH ≥40 IU/L and 7 had <40 IU/L. Whereas out of 44 premenopausal females 20 had FSH≥40 IU/L and 24 with <40 IU/L.
As calculated serum FSH ≥40 IU/L in detecting postmenopausal status of the female had a sensitivity of 95.36% and specificity of 54.55%.

Table 8: Distribution of subjects according to groups.

Groups	Number of subjects	Percent
FSH<40 and pH <4.5	18	9
FSH <40 and pH ≥4.5	2	1
FSH ≥40 and pH <4.5	7	3.5
FSH ≥40and pH ≥ 4.5	173	86.5
Total	200	100

In our study, out of 200 subjects, 180 had FSH ≥40 IU/L out of which 7 had pH< 4.5 and 173 ≥4.5. Rest 20 had FSH had <40 IU/L including with pH <4.5 and 2 with pH ≥4.5.
In our study, both vaginal pH and serum FSH were found to be positively associated by Pearson Chi-square test(p<0.001). Also the changes are equally likely by Mcnemer test (p=0.180).
Vaginal pH and serum FSH were observed to be positively correlated with a Pearson Coefficient of 0.862 and Spearman's rho 0.879 and p <0.001.

DISCUSSION

The mean age of subjects in our study was 51.59±5.648 years with minimum age of 40 years and maximum age of 65 years. This is comparable to the study done by Kaur K et al (52.64±7.57), Moradon S et al (58±3.8).[20,21]
The mean age of our subjects attaining menopause was 48.48± 2.29 years which is similar to studies conducted in India by Panda S et al (47.8±4.1) and Kaur k et al (47.42±3.64).[20,22]
Mean pH of subjects in our study was 5.5±1.03 which is comparable to the studies done by Yoruk P et al (5.9±0.95),[14] Panda Set al (5.3±0.7).[22]
In our study, with the cutoff value of vaginal pH taken as >4.5, the sensitivity of vaginal pH in diagnosis of menopause was 96.11%.
According to the study conducted by Caillouette JC et al,[19] elevated pH level in the range of 5-6.5 suggests a diagnosis of bacterial pathogens or decreased serum estradiol and in the absence of bacterial agents, pH range of 6-7.5 suggests menopause. They reported that the sensitivity of vaginal pH in predicting estradiol status was 88% and positive predictive value was 96% which is in accordance with our results.
Moradon S et al,[21] also observed that vaginal pH in diagnosis of menopause has a sensitivity of 92.7%.
According to the study conducted by Panda S et al,[22] sensitivity of vaginal pH > 4.5 for menopausal diagnosis was 84.9%.The results in studies mentioned above are consistent with our results.
In our study, the cut off level serum FSH≥40IU/L was taken for the diagnosis of menopause.
Panda S et al,[22] took serum FSH level≥40 IU/L as the cutoff value for the diagnosis of menopause in their study. Also in the study conducted by Kaur K et al [20] serum FSH≥40 IU/L was taken as the diagnostic cutoff for menopausal status.
These cutoff levels of serum FSH are similar to the cutoff point used in our study.
Moradon S et al,[21] took serum FSH ≥35 IU/L as the cutoff point for diagnosing menopause in their study.
The mean serum FSH of the subjects in our study was 56.24±14.6IU/L. In the studies conducted by Yoruk P et al,[14] and Panda S et al,[22] the mean serum FSH was 53.3±32.8 IU/L and 46.5±11 IU/L respectively. These levels are in accordance with our study
In our study, the sensitivity of serum FSH to diagnose menopause was 95.36% when the cut off level of serum FSH was taken as 40IU/L.
In the study conducted by Panda S et al,[22] the sensitivity of serum FSH≥40IU/L as diagnostic of menopause was 77.4%. Roy S et al,[23] in their study, observed that the sensitivity of serum FSH in diagnosing low estradiol status in menopausal women was 68%. These have lesser sensitivity than ours.
In our study, with serum FSH≥40IU/L taken as cut off point for the diagnosis of menopause, a vaginal pH> 4.5 showed a sensitivity of 96.11% in diagnosing menopause.
Roy S et al,[23] in a review article study analysed 16 studies and concluded that in women without vaginitis and no estrogen therapy, a vaginal pH of >4.5 indicated menopause, because it demonstrated a similar sensitivity (64-67%) as FSH in epidemiologic studies.
It was concluded by Azzam AZ et al., (2005),[11] in their study, that the average estradiol value for women with PH> 4.5 was 22.18±5.98pg/ml. The average FSH value for perimenopausal women was 44.24±7.4. In the absence of vaginitis, an elevated vaginal pH>4.5 and serum FSH≥40IU/L are good predictors of low estradiol level with nearly similar sensitivity and accuracy.
The classifications over vaginal pH and FSH are positively associated by Pearson Chi-square test, i.e. p<0.001. And the changes are equally likely by McNemer test (p=0.180). Their agreement by Kappa statistic is also significant (value=0.775 and p<0.001). Spearman's rho had a correlation

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coefficient of 0.879 and p<0.001, showing that the two parameters serum FSH and Vaginal pH are positively correlated.

Similar to our study, in a study conducted by Kadhum TJ et al,[24] it was observed that the sensitivities of vaginal pH and serum FSH were comparable (p=0.516) denoting their similarity for diagnosing menopause. The correlation between vaginal pH and FSH and estradiol levels were seen.

CONCLUSION

Vaginal pH is a simple, accurate, non-invasive and cost-effective office tool that can be used as an alternative to S.FSH for diagnosis of menopause. Earlier the diagnosis, earlier we can initiate the treatment and better the quality of life.

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