

## Vaginal pH as a Diagnostic Tool for Menopause: A Preliminary Analysis

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## ABSTRACT

**Introduction:** Menopause is defined as the permanent cessation of menstruation, as a result of decrease in ovarian follicles and the loss of ovarian activity. There is decrease in inhibin B level which causes decrease in negative feedback on the serum follicle-stimulating hormone (FSH), which in turn increases the level of serum FSH. Serum FSH is routinely used as a marker of menopause. Decline in the estrogen level causes thinning of vaginal epithelium, resulting in less exfoliation of the vaginal epithelial cells, lesser available glycogen, and decreased substrate for acid production, leading to increase in vaginal pH. **Aims:** The aim of this study is to compare the sensitivity of vaginal pH versus serum FSH level to diagnose menopause. **Settings and Design:** This is a cross-sectional study, performed in obstetrics and gynecology outpatient department of a teaching hospital of central Gujarat. **Subjects and Methods:** A total of 120 women who had their last menstrual period >1 year back (menopause) were included in the study. Vaginal pH was measured and serum sample was taken to measure FSH level. Sensitivity of both vaginal pH and serum FSH to diagnose menopause was compared. McNemar test was used to analyze the convergence of the two methods for the diagnosis of menopause. **Results:** In the absence of vaginal infection, sensitivity of vaginal pH to diagnose menopause was 90%, while sensitivity of the serum FSH was 85%. **Conclusions:** Sensitivity of the vaginal pH is similar to the serum FSH for diagnosis of menopause.

**KEYWORDS:** Cross-sectional studies, follicle-stimulating hormone, menopause, vagina

## INTRODUCTION

Menopause is defined as “the permanent cessation of menstruation as a result of the loss of ovarian activity” (WHO).<sup>[1]</sup> Stoppage of menstruation for 12 consecutive months without any other pathology is clinically defined as menopause. Hence, a woman is declared to have attained menopause only retrospectively. The average age of menopause worldwide is 45–51 years,<sup>[2]</sup> while in India, it is 41.3–51.1 years.<sup>[3]</sup>

In menopause, there is loss of ovarian follicular activity and decrease in the number of follicles which is associated with decrease in the serum inhibin B levels, which causes a decrease in negative feedback on the serum follicle-stimulating hormone (FSH), in turn enabling serum FSH levels to increase. Hence, serum FSH is an established indirect marker of the follicular activity.<sup>[4]</sup>

Normally, when vaginal epithelial cells exfoliate and die, they release glycogen which is hydrolyzed to glucose and broken down into lactic acid by *Lactobacillus*, which is normal vaginal commensal organism.<sup>[5]</sup> This mechanism also helps to maintain acidic pH in the reproductive age group women. In menopause, estrogen level declines which causes thinning of the vaginal epithelium, resulting in less exfoliation of vaginal epithelial cells, lesser available glycogen, and decreased substrate for acid production, leading to increase in the vaginal pH.<sup>[6]</sup>

Diagnosis of menopause can be made by the presence of mainly vasomotor and/or urogenital symptoms and signs

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of urogenital atrophy. Vaginal ultrasound to measure ovarian volume and number of antral follicles also help in the diagnosis. Serum level of FSH >40 IU/L is usually used to confirm diagnosis of menopause.<sup>[7]</sup> FSH is elevated even before the onset of symptoms. However, this is an expensive test and many patients cannot afford it.

Normal vaginal pH is <4.5 which can increase in the presence of vaginal infection.<sup>[8]</sup> In the absence of vaginal infection, a pH level >4.5 strongly suggests decreasing levels of estrogen. Hence, pH measurement in the absence of vaginal infections may be used to diagnose menopause.<sup>[9]</sup> A few authors so far have suggested vaginal pH as a more cost-effective, simple, and noninvasive method to diagnose menopause.<sup>[10]</sup>

The present study was carried out with the objective of comparing sensitivity of vaginal pH with serum FSH levels to diagnose menopause.

## SUBJECTS AND METHODS

A cross-sectional study was performed in the gynecology outpatient department of a teaching hospital of Central Gujarat from November 2018 to November 2019 after approval of institutional ethics committee. A total of 120 women aged 35–75 years who had their last menstrual period >1 year back (menopause) and who are willing to give written informed consent were included in the study. All other causes of amenorrhea were excluded. Complete demographic characteristics (age, parity and body mass index [BMI]), menstrual, sexual, medical, and family history of early menopause and other gynecological disorder) and clinical manifestation of menopause were obtained. Exclusion criteria comprised of pregnancy, postpartum period, ongoing hormone replacement therapy, menopause due to chemotherapy or radiotherapy, sexual intercourse within the previous 3 days, uses of estrogen gel, vaginal douches, uses of vaginal lubricants, and vaginal bleeding.

All of them were screened for vaginal infection by taking vaginal swab. Those who were positive for any of the infective agent were treated and called back after 3 weeks. Once their swab report was negative, vaginal pH was measured. During vaginal examination, after the insertion of a nonlubricated sterile vaginal speculum, 4 cm micro-range pH strip was applied directly to the lateral vaginal wall at the outer third of the vagina until it became wet. Color changes of the strip were immediately compared with the colorimetric scale, and the measurements were recorded. Transvaginal sonography was done to exclude other pelvic pathology. Serum sample was taken and serum FSH level was

measured using radioimmunoassay in designated laboratory. Values of vaginal pH and serum FSH were noted.

After data collection, statistical analysis was performed using Statistical Package for the Social Sciences software version 21.0 (IBM corporation, Armonk, New York, USA). McNemar test was used to analyze the convergence of the two methods for the diagnosis of menopause.

## RESULTS

In the present study, 63.33% of the participants belonged to 49–61 years of age group and only 16.67% of the participants belonged to 62–75 years of age. Majority (81.67%) of the participants were Hindus and 65.83% of the participants belonged to urban area. Majority (60.83%) of the participants had normal BMI, 38.33% of the participants were overweight, and only one out of 120 participants was obese. Around 60% of the participants belonged to middle socioeconomic class [Table 1].

Mean vaginal pH of the participants was  $6.14 \pm 1.13$  with standard deviation of 1.13 (range 6–7) [Table 2]. Mean serum FSH value of the participants was  $73.14 \pm 32$  with standard deviation of 32 (range 49.080–92.865) [Table 3]. Sensitivity of the vaginal pH and the serum FSH for predicting menopause was 90% and 85%, respectively [Figure 1]. While comparing vaginal pH and serum FSH levels, no significant difference was seen in their sensitivity to diagnose menopause using McNemar test. ( $P > 0.05$ ) [Table 4].

According to our results, to diagnose menopause, vaginal pH has specificity of 44%, positive predictive value of 91%, negative predictive value of 67%, positive likelihood ratio of 1.72, and negative likelihood ratio of 0.088 (cutoff value pH >4.5 and FSH >40 IU/L)

**Table 1: Sociodemographic parameters of participants**

Sociodemographic parameters	Categories	Frequency (%)
Age distribution in years	35-48	24 (20.00)
	49-61	76 (63.33)
	62-75	20 (16.67)
Religion	Hindu	98 (81.67)
	Muslim	22 (18.33)
Locality	Rural	41 (34.17)
	Urban	79 (65.83)
BMI (kg/m <sup>2</sup> )	18.5-24.9	73 (60.83)
	25.29.9	46 (38.33)
	>30	1 (0.83)
Socioeconomical status	Lower	32 (26.67)
	Middle	72 (60.00)
	Upper	16 (13.33)

BMI: Body mass index

**Table 2: Distribution of participants according to vaginal pH**

pH	Frequency (%)
≤4.5	12 (10.00)
>4.5	108 (90.00)
Mean±SD	6.14±1.13
Median (IQR)	6 (6-7)

SD: Standard deviation, IQR: Interquartile range

**Table 3: Distribution of participants according to serum follicle-stimulating hormone**

Serum FSH	Frequency (%)
≤40	18 (15.00)
>40	102 (85.00)
Mean±SD	73.14±32
Median (IQR)	69.27 (49.080-92.865)

FSH: Follicle-stimulating hormone, SD: Standard deviation, IQR: Interquartile range

**Table 4: Comparison of sensitivity of pH and serum follicle-stimulating hormone for predicting menopause**

pH	Serum FSH		Total, n (%)	P
	≤40 (n=18), n (%)	>40 (n=108), n (%)		
≤4.5	8 (6.67)	4 (3.33)	12 (10.00)	0.180*
>4.5	10 (8.33)	98 (81.67)	108 (90.00)	
Total	18 (15.00)	102 (85.00)	120 (100.00)	

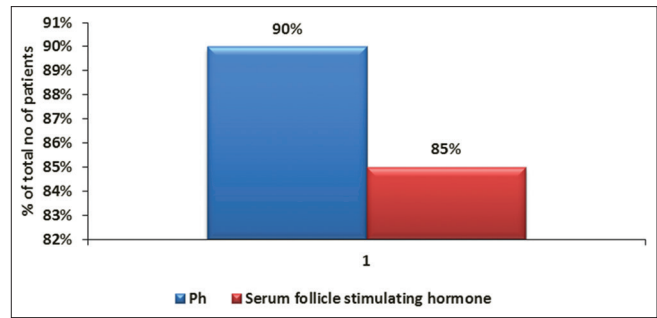
\*McNemar test. FSH: Follicle-stimulating hormone

## DISCUSSION

Natural menopause is defined as the permanent cessation of menstruation, resulting from the loss of ovarian follicular activity. It is recognized to have occurred after 12 consecutive months of amenorrhea, for which there is no other obvious pathologic or physiologic cause.<sup>[11]</sup>

The period immediately before and up to 1 year after the final menstrual period is known as perimenopause. The characteristics are increased blood levels of FSH, decrease in circulating estrogen levels, anovulatory cycles, significantly reduced fertility and erratic menstrual periods, and onset of urogenital symptoms.<sup>[12-14]</sup>

Serum FSH level measurement is generally used for diagnosis of menopause; the value considered to diagnose menopause is 40 mIU/ml.<sup>[7]</sup> Stellato *et al.* indicated that FSH alone cannot differentiate between perimenopausal and postmenopausal period. FSH cutoff of 40 IU/L is inappropriate for clinical determination of postmenopausal status, according to their study.<sup>[15]</sup> Henrich *et al.* demonstrated that serum FSH has limited utility to distinguish between different menopausal stages.<sup>[16]</sup> In another study, Burger showed that both

**Figure 1: Sensitivity of pH and serum follicle-stimulating hormone**

serum FSH and LH were of little diagnostic value in the assessment of menopause.<sup>[17]</sup>

Moreover, Gow *et al.* indicated that biochemical parameters do not guarantee menopausal status and cannot distinguish the early postmenopausal period from the period preceding menopause.<sup>[18]</sup>

Shin *et al.* assessed various hormonal markers (oestradiol, FSH, Anti-Mullerian Hormone (AMH), and inhibin) to determine menopausal status for 144 women. They showed that the sensitivity of serum FSH to diagnose menopause was 99.1% and the specificity was 97%.<sup>[19]</sup> We had conducted study in 120 menopausal participants of age group of 35–75 years, and in our study, the sensitivity of serum FSH to diagnose menopause is 85% (cutoff level >40 mIU/ml).

At menopause, with declining levels of estrogen, the vaginal epithelium thins. Fewer epithelial cells result in less exfoliation of the cells into the vagina, which in turn give rise to increase in vaginal pH. This results into loss of lactobacilli and an overgrowth of other bacteria, resulting into symptomatic urogenital infections.<sup>[5,20]</sup>

In a large epidemiologic study conducted in Costa Rica, it was indicated that vaginal pH is strongly related to age and to menopausal status and thus could be a marker of menopause. They reported that vaginal pH >5 has a sensitivity of 64%–67% for the diagnosis of menopause.<sup>[21]</sup> In our study, the sensitivity of vaginal pH to diagnose menopause is 90% (cutoff value pH >4.5). Cailloutte *et al.* in their study reported that in the absence of vaginitis, a vaginal pH >4.5 indicated menopause with a sensitivity of 74%.<sup>[22]</sup> Another study suggested that in the absence of vaginitis, the sensitivity of vaginal pH for menopausal diagnosis was 97% (cutoff level of pH >4.5).<sup>[23]</sup>

Roy *et al.* assessed vaginal pH and serum FSH level among 172 postmenopausal women and concluded that a vaginal pH of >4.5 has a similar sensitivity as FSH for diagnosis of menopause. They reported that the sensitivity of vaginal pH in predicting estradiol status

was 88%.<sup>[24]</sup> Moradan *et al.* reported that vaginal pH in the diagnosis of menopause has a sensitivity of 92.7% and a specificity of 83.5%, with taking cutoff value of pH >6.<sup>[9]</sup> In another study of 173 menopausal women, the sensitivity of vaginal pH for menopausal diagnosis was 84.9% and of serum FSH was 77.4% (cutoff level vaginal pH >4.5 and serum FSH  $\geq$ 40 IU/L).<sup>[10]</sup> In the present study, the sensitivity of vaginal pH for diagnosis of menopause is 90% and positive predictive value is 90.74%, while the sensitivity of serum FSH to diagnose menopause is 85%.(cutoff value pH >4.5 and serum FSH >40 mIU/ml).

## CONCLUSION

This concludes that vaginal pH has similar sensitivity as of the serum FSH levels to diagnose menopause.

The study has a few limitations. It is a hospital-based study, so the results cannot be extrapolated to the general population. Being a cross-sectional study, long-term follow-up data of the participants are not available.

Further studies with larger population are recommended to validate our result which may establish vaginal pH measurement as a reliable replacement for serum FSH measurement for diagnosing menopause.

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## Conflicts of interest

There are no conflicts of interest.

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