НИРКИ KIDNEYS

DOI: https://doi.org/10.22141/2307-1257.14.2.2025.524

Hawraa Nasser Hamza, Hanaa Ali Aziz, Dhay Ali Azeez
College of Science, Al-Muthanna University, Samawa, Iraq

Physiologic-microbiome interactions in the pathogenesis of genitourinary syndrome of menopause among menopausal stages

For citation: Kidneys. 2025;14(2):147-153. doi: 10.22141/2307-1257.14.2.2025.524

Abstract. ***Background.*** *Menopause is a natural decline in ovarian function, leading to reduced estrogen and progesterone levels. It occurs in three stages: peri-menopause, menopause, and post-menopause. Estrogen plays a crucial role in maintaining the integrity and microbial balance of the vaginal microenvironment. Physiological and microbiome alterations throughout the menopausal stages contribute to the severity of genitourinary syndrome of menopause (GSM), which encompasses a range of symptoms affecting the vagina, bladder, and urethra. The purpose was to investigate the correlation between hormonal fluctuations and vaginal microbiome alterations, as well as their role in the severity of GSM.* ***Materials and methods.*** *This study was conducted from September to December 2024, involving 100 participants: 75 post-menopausal women (aged 45 and older) at various time intervals since their last menstruation, and 25 pre-menopausal women under 40 with regular menstrual cycles. Clinical checkups were performed before sample collection. Hormonal concentrations were measured using the BIOT-YG-I FIA immunoassay analyzer, while microbial isolates were identified using CHROMagar media.* ***Results.*** *A significant difference in estradiol-2 was found: in pre-menopausal women, its level was 179.17 ± 14.21 compared to 64.72 ± 8.53 in peri-menopausal, 28.75 ± 3.49 in menopausal, and 24.50 ± 2.46 in post-menopausal participants. Progesterone level was 0.65 ± 0.06 in pre-menopausal women, 0.370 ± 0.018 in peri-menopausal, in menopausal group — 0.340 ± 0.017, and 0.304 ± 0.017 in post-menopausal. The mean level of follicle-stimulating hormone was lower in pre-menopausal participants — 5.22 ± 0.90 versus 79.00 ± 7.49 in peri-menopause group, 89.72 ± 8.70 in menopause, and 94.17 ± 9.77 in post-menopausal women. Testosterone mean level was higher in pre-menopausal participants — 0.63 ± 0.06 compared to 0.480 ± 0.089 in peri-menopausal participants, 0.480 ± 0.078 in menopausal, and for post-menopause group, it was 0.610 ± 0.091. L.acidophilus proportion isolated from vaginal swab sample was 12.0 % in peri-menopausal participants, 16.0 % in menopausal, 24.0 % in post-menopausal, and 52.0 % in pre-menopause group. In addition, the most isolated bacterial pathogen was E.faecalis, the rates were 64.0 % for peri-menopausal, 56.0 % for menopausal, 60.0 % for post-menopausal and 12.0 % for pre-menopausal participants. In menopause and post-menopause groups, there was significant association between urogenital symptoms and bacterial growth (P > 0.05).* ***Conclusions.*** *Estradiol-2 and progesterone levels progressively decline from peri-menopause to post-menopause, reaching baseline levels. Bacterial diversity is more pronounced in post-menopausal women compared to pre-menopausal participants. Furthermore, in post-menopausal women, a significant correlation was observed between bacterial colonization and the emergence of urogenital symptoms, supporting the link between altered vaginal microbiota and GSM severity.*

Keywords: *sex hormones; menopause; genitourinary syndrome of menopause; Lactobacillus; E.faecalis*

Introduction

Menopause involves the loss of ovarian reproductive activity, either naturally or as a result of other disorders. Debilitating physical symptoms, such as hot flashes and night sweats, urogenital atrophy, sexual dysfunction, mood swings, bone loss, and metabolic abnormalities that increase the risk of diabetes and cardiovascular disease, might result from the decrease in ovarian estrogen production during menopause [1]. However, women life stages classified to pre-menopausal phase is considered the reproductive phase which the ovulation is regular and the ovaries completely functional and its starting at puberty, a peri-menopause is

For correspondence: Hanaa Ali Aziz, College of Science, Al-Muthanna University, Samawa, Iraq; e-mail: Hanabio-1983@mu.edu.iq
Full list of authors' information is available at the end of the article.

a transitional phase when female hormones levels especially estrogen start to decline leading to irregular period and reduction in ovaries hormones role [2]. Menopause phase represent a 12 months without amenorrhea and has two types a natural menopause and sudden or induced menopause due to surgeries or medical treatments [3]. A post-menopausal phase following the menopause and last to the rest of women life [4].

Genitourinary syndrome of menopause is a modern terminology for vulvovaginal atrophy, or urogenital atrophy, defined as a set of chronic and progressive conditions results from a deficiency in estrogen hormone levels and other sex steroids [5], this syndrome characterized by a several symptoms include a physical changes effecting the labia majora and minora, clitoris, vestibule, introitus, vagina, urethra, and bladder, and another genital symptoms like dryness, burning, and irritation, a sexual symptoms include reduced lubrication, pain, low libido, dyspareunia, and a urinary problems like urinary incontinence, recurrent urination, painful urination, and recurrent urinary tract infections. Which resulting from an over-growth of the opportunistic microbes [6].

The vagina colonized by a diverse range of microorganisms that make up the mycobiota and microbiota. *Lactobacillus* spp. is the most frequent microorganism that isolated from healthy human vagina, which also known as lactic acid bacteria (LAB) [7]. These vaginal *Lactobacilli* have been hailed for their ability to prevent pathogens invasion by maintaining a healthy population, by producing lactic acid and secreting a various antimicrobial ingredients such as H_2O_2, cytokines, and surfactants [8].

Vaginal microbiota structure and abundance are influenced by estrogen and progesterone, that are starting at puberty and continue through a reproductive years in a dynamic equilibrium with some variations [9]. Estrogen promote the proliferation of a vaginal epithelial cells and rise in glycogen storage, while a progesterone lyses the epithelial cells of vagina, thus facilitating release of glycogen to maintain the normal pH [10]. Wherefore, there is a notable increase in anaerobic bacteria and vaginosis related bacteria such as (*E.faecalis*, *E.coli*, *S.aureus*, *C.albicans*, etc.) that have role in existence of several urogenital symptoms includes vaginal dryness, burning, itching, irritation, and discharges [5].

The purpose of this study was to investigate about the correlation that associate the alternations occur in some female hormones and their participation in vaginal microbiome incompetence and how can genitourinary syndrome of menopause take a place, for enhancing the diagnostic strategies and improving GSM targeted therapies.

Materials and methods

The present study is conducted between July and December 2024 Maternity and Pediatric Hospital and private gynecology clinic in Al-Muthanna (Iraq). The included 100 participants women, divided in to four groups according to last menstrual cycle, group 1: participants women with continuous menstrual cycle (25 pre-menopause) with age range 20–40 years, group 2: participants women with less than 1 years last menstrual cycle (25 peri-menopause) with age between 45 and 50 years, group 3: participants women with 1 to less than 2 years last menstrual cycle (25 menopause), their age was 45–55 years. In addition to, 25 participants women with more than 2 years last menstrual cycle (25 post-menopause) from 50 age and more. Those who had undergone hysterectomy or oophorectomy, and pregnancy women were excluded.

BIOT-YG-I FIA immunoassay analyzer is used to measure the quantitative concentration of serum blood sample by a fluorescence immunoassay system. Was used to determine the hormonal concentration of estradiol-2, progesterone, follicle-stimulating hormone and testosterone.

5 ml of blood sample for determination of hormonal parameters, vaginal swab sample, and mid-stream urine sample was obtained and stored at 2–8 °C inside safety box until reach to the lab.

Selective media utilized to diagnosis a different bacterial species. HiCrome Lactobacillus selective agar use for isolation and differentiation between different species of *Lactobacillus*, HiCrome UTI agar media facilitates and accelerate the identification of some gram-positive bacteria and some gram- negative bacteria based on the difference in the shape and color of the colonies. HiCrome Candida differential agar media is recommendation for ease identification and isolation of *Candida* spp.

Ethical approval

The principles summarized in the Declaration of Helsinki which served as the basis for conduction of this study. Verbal consent was acquired and the questionnaire form was registered from the participants prior to obtaining the samples. The study protocol examined and approved by a local ethics committee.

Statistical analysis

Statistical analysis is conducted using SPSS (Statistical Package for the Social Sciences) version 24. Mean of the data between more than two groups was assessed by using ANOVA, Pearson correlation coefficient was used to assess a correlation between two numeric variables, and the chi-square test is applied to examine an association between the categorical variables. The level of significance was set at a $P \leq 0.05$ and the highly significant level was considered at $P \leq 0.01$.

Results

Hormonal parameters

The mean level of estradiol-2 (E2) was higher in pre-menopause participants compared to other groups and the difference was highly significant ($P < 0.001$). Also, there was a significant decrease in menopause participants and post-menopause participants compared to peri-menopause participants.

Progesterone mean level was higher in pre-menopause participants compared to other groups and the difference was highly significant ($P < 0.001$). But there was non-significant difference in other groups of participants.

The mean levels of follicle-stimulating hormone (FSH), it was lower in pre-menopause participants compared

to other groups and the difference was highly significant ($P < 0.001$). But there was non-significant difference in other groups of participants.

Testosterone mean level was higher in pre-menopause participants compared to other groups and the difference was non-significant ($P = 0.392$) (Table 1).

Microbial results

The comparison between different pre-menopausal, peri-menopausal, menopausal and post-menopausal participants according to bacterial growth in vaginal swab culture were carried and the results show in Fig. 1. The diverse bacterial growth rates were shown at 84.0 % in peri-menopausal, 76.0 % in menopausal, and 92.0 % post-menopausal participants respectively compared to only 12.0 % of pre-menopausal participants was diverse growth ($P = 0.001$).

The proportion of *Lactobacillus* spp. that obtained from vaginal swab samples characterized by their low levels in menopausal groups, as shown in Table 2. *L.acidophilus* proportion in peri-menopausal participants was 12.0 %, menopausal 16.0 %, and 24.0 % in post-menopausal group compared to 52.0 % in pre-menopausal participants and the difference was significant ($p = 0.025$) (Fig. 4).

The most isolated bacterial pathogen from vaginal swab culture was *E.faecalis*, and the rates were 64.0 % for peri-menopausal, 56.0 % in menopausal, and 60.0 % for post-menopausal participants respectively, compared to pre-menopausal (12.0 %) participants ($P = 0.027$). Followed by *E.coli, S.aureus*, and *C.albicans*, as shown in Table 2, Fig. 3.

The bacterial growth rates from urine sample were shown in Fig. 2. 92.0 % in peri-menopausal, 100.0 % menopausal, and 88.0 % post-menopausal participants respectively compared to only 36.0 % of pre-menopausal participants was microbial growth ($P = 0.001$). And the most isolated bacterial pathogen was *E.faecalis*, the rates were 64.0, 44.0, and 52.0 % for peri-menopausal, menopausal and post-menopausal participants respectively compared to pre-menopausal (12.0 %) participants ($P = 0.035$), and as demonstrated in Table 3.

Table 4 shows the association between urogenital symptoms that are related with genitourinary syndrome (GSM) and bacterial growth in vaginal swab culture, that has been carried out. The present results show there was non-significant association between urogenital symptoms and bacterial growth type in peri-menopause group ($P < 0.05$). But in menopause and post-menopause groups, there was significant association between urogenital symptoms and bacterial growth ($P > 0.05$).

Discussion

Several previous studies [11, 12], confirms this study results about serum estradiol-2 levels of the menopausal women. Found the serum E2 at high levels during pre-menopause stage, which is regulate the ovulation and fertility that is production predominate the follicular phase [13]. Erratic ovarian function and the cycle irregularity during a peri-menopause stage, spikes the E2 level and begin to demonstrate vasomotor symptoms. The lowest levels of E2 through post-menopausal stage. As a result, ovarian functions bring to halt progesterone levels are rise through the reproductive years, especially during luteal phase after ovulation, as progesterone is produced by corpus luteum, and it becomes low in the follicular phase. At peri-menopause the progesterone level fluctuates and generally decreases due to irregular menstruation and deficiencies in luteal phase. The progesterone drop to a baseline at the post-menopausal stage as the ovaries function being ceased [14, 15].

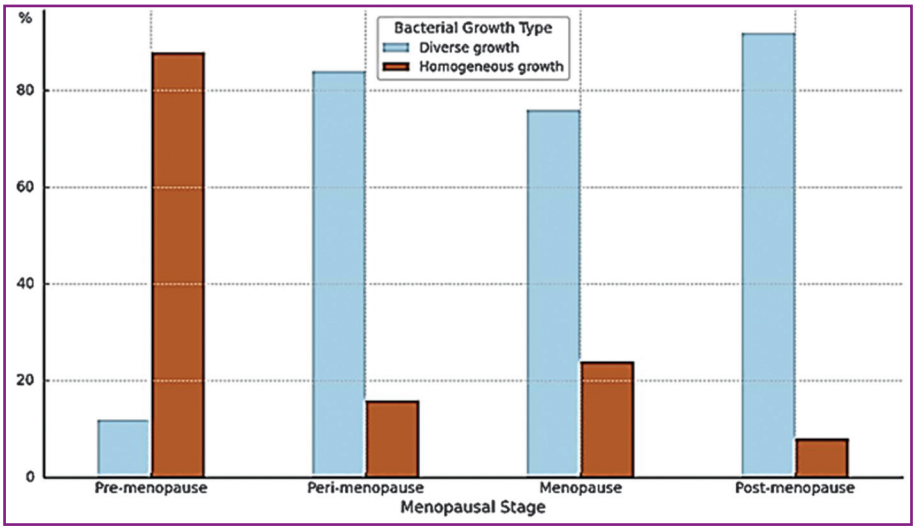

Figure 1. Bacterial growth type in pre-menopausal, peri-menopausal, menopausal and post-menopausal women of vaginal swab culture

Table 1. Estradiol-2, progesterone, follicle-stimulating hormone, and testosterone levels

Groups		E2 (pg/ml)	Progesterone (ng/ml)	FSH (mIU/ml)	Testosterone (ng/ml)
Pre-menopause	Mean ± SE	179.17 ± 14.21	0.65 ± 0.06	5.22 ± 0.90	0.63 ± 0.06
Peri-menopause		64.72 ± 8.53	0.372 ± 0.018	79.00 ± 7.49	0.480 ± 0.089
Menopause		28.75 ± 3.49	0.344 ± 0.017	89.72 ± 8.70	0.480 ± 0.078
Post-menopause		24.50 ± 2.46	0.304 ± 0.017	94.17 ± 9.77	0.610 ± 0.091
P-value		0.001	0.001	0.001	0.392

FSH levels are low at reproductive phase in pre-menopausal women through their follicular phase (day 2, 3, or 4) FSH promotes the follicle growth inside the ovary, but during luteal phase the feedback mechanism of estrogen and progesterone lowers FSH level. At peri-menopause life stage the ovarian reserve is declines and a menses irregular, causing increase or fluctuate in FSH levels due to reduced negative feedback process that is loss through the post-menopausal stage, leading to sustained high levels of FSH [16, 17]. The higher mean of testosterone at pre-menopausal women reflect an active ovarian and adrenal function, supporting muscle mass, libido, mood, and bone density, and a gradual decline in testosterone level began at peri-menopause as ovarian function being irregular, until its showed at lowest level after menopause, ovarian dysfunction and adrenal insufficiency, involved in decline the levels of testosterone, resulting in low libido, loss muscle mass, rise the osteoporosis risk, and mood swing, anxiety, or depression [18].

The transition from the menstrual phase to follicular phase, sex hormones start to rise and epithelial cells of

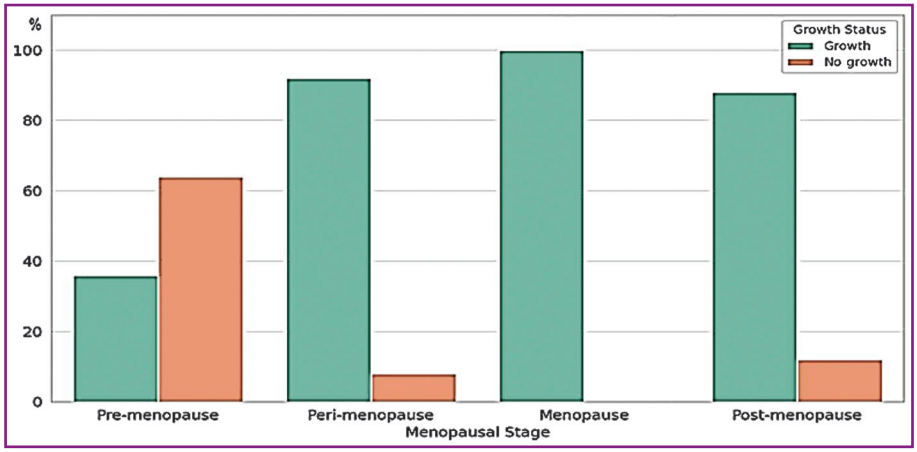

Figure 2. Bacterial growth in pre-menopausal, peri-menopausal, menopausal and post-menopausal women of urine sample

Table 2. Frequency distribution of specific bacterial isolation from pre-menopausal and post-menopausal women in vaginal swab culture, n (%)

Microbial species	Pre-menopause	Peri-menopause	Menopause	Post-menopause	P-value
L.acidophilus	13 (52.0)	3 (12.0)	4 (16.0)	6 (24.0)	0.025
L.rhamnosus	16 (64.0)	7 (28.0)	9 (36.0)	6 (24.0)	0.093
L.plantarum	2 (8.0)	2 (8.0)	5 (20.0)	1 (4.0)	0.308
L.fermentum	8 (32.0)	1 (4.0)	1 (4.0)	2 (8.0)	0.010
E.faecalis	3 (12.0)	16 (64.0)	14 (56.0)	15 (60.0)	0.027
E.coli	3 (12.0)	17 (68.0)	13 (52.0)	11 (44.0)	0.024
C.krusei	4 (16.0)	0	2 (8.0)	1 (4.0)	0.328
C.glabrata	3 (12.0)	0	0	0	
C.albicans	3 (12.0)	6 (24.0)	1 (4.0)	7 (28.0)	0.148
S.aureus	0	2 (8.0)	8 (32.0)	7 (28.0)	0.036
K.pneumoniae	0	7 (28.0)	2 (8.0)	5 (20.0)	0.092
P.aeruginosa	0	2 (8.0)	2 (8.0)	1 (4.0)	0.819
B.cereus	0			1 (4.0)	

Table 3. Frequency distribution of specific bacterial isolations in pre-menopausal and post-menopausal women in urine samples, n (%)

Bacterial species	Pre-menopause	Peri-menopause	Menopause	Post-menopause	P-value
P.mirabilis	0	0	1 (4.0)	1 (4.0)	
E.faecalis	3 (12.0)	16 (64.0)	11 (44.0)	13 (52.0)	0.035
E.coli	5 (20.0)	14 (56.0)	10 (40.0)	11 (44.0)	0.241
C.krusei	0	0	1 (4.0)	1 (4.0)	
S.epidermidis	0	0	6 (24.0)	1 (4.0)	0.059
C.albicans	0	1 (4.0)	0	3 (12.0)	0.317
S.aureus	0	2 (8.0)	6 (24.0)	5 (20.0)	0.368
K.pneumoniae	0	6 (24.0)	2 (8.0)	1 (4.0)	0.097
P.aeruginosa	0	4 (16.0)	0	0	
B.cereus	0	0	1 (4.0)	3 (12.0)	

the vaginal wall gradually thicken and release more glycogen, which lyses to produce lactic acid, that lowering the pH of vagina and support the proliferation of *Lactobacillus* spp., particularly *L.acidophilus*. With peri-menopausal, menopausal, post-menopausal women, there appears to being a reduction in lactobacilli, which associated with a significant changes in reproductive hormones, includes lowers in estrogen levels and a higher serum levels of FSH levels. Lead to show a diversity of another anaerobic bacteria [19].

The high prevalence of *E.faecalis* from vaginal isolated samples could be due to the significant virulence factors of this bacterial species including biofilm formation and a capacity to adherence to the urogenital tracts, a wide ability to survive in severe environments [20]. Additionally to, many of *E.faecalis* strains considered as multi-drug resistance including the cephalosporins [21]. Due to the menopausal physiological changes, the vaginal tract microenvironment was represented as a reservoir to the uropathogenic *E.coli* colonization, which contributing in vaginal infections and recurrent UTIs [22]. Opportunistic infections by *S.aureus* and *C.albicans* in menopausal women was also presented due to hormonal changes, reduction in immune response, and mucosal alternations which leading to microbial overgrowth and imbalance. Resulting in an aerobic vaginitis and vulvovaginal candidiasis [23].

After menopause, reduction in serum level of E2, decline in progesterone level, and increase in serum level of follicle-stimulating hormone, leading to thinning of the urogenital tracts epithelium, reduce in vaginal lubrication,

Table 4. Association between some urogenital symptoms related to GSM and the bacterial growth in vaginal swab culture, n (%)

Groups		Frequent urination	Burning	Itching	Genital irritation	Vaginal discharges	Vaginal dryness
Pre-menopause	Diverse	3 (37.5)	3 (37.5)	2 (33.3)	3 (75.0)	3 (23.1)	3 (75.0)
	Homogenous	5 (62.5)	5 (62.5)	4 (66.7)	1 (25.0)	10 (76.9)	1 (25.0)
P-value		0.480	0.480	0.414	0.137	0.052	0.137
Peri-menopause	Diverse	18 (94.7)	14 (87.5)	11 (100)	12 (100)	14 (87.5)	10 (90.9)
	Homogenous	1 (5.3)	2 (12.5)	0	0	2 (12.5)	1 (9.1)
P-value		0.001	0.003	0.001	0.001	0.003	0.001
Menopause	Diverse	13 (86.7)	14 (100)	11 (91.7)	12 (100)	7 (87.5)	16 (88.9)
	Homogenous	2 (13.3)	0	1 (8.3)	0	1 (1.5)	2 (11.1)
P-value		0.005	0.001	0.004	0.001	0.034	0.001
Post-menopause	Diverse	19 (95.0)	16 (94.1)	12 (100)	11 (84.6)	4 (80.0)	20 (90.9)
	Homogenous	1 (5.0)	1 (5.9)	0	2 (15.4)	1 (20.0)	2 (9.1)
P-value		0.001	0.001	0.001	0.013	0.108	0.001

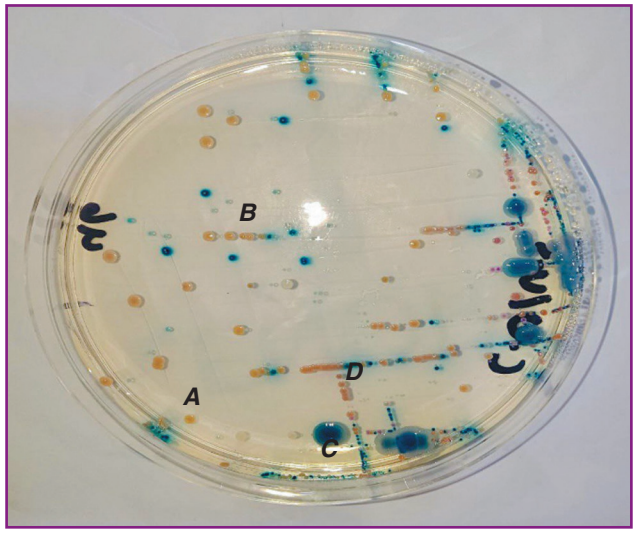

Figure 3. The bacterial isolates on HiCrome UTI agar: A — golden yellow colonies are S.aureus; B — E.faecalis in blue small colonies; C — blue-purple mucoid colonies are K.pneumoniae; D — pink colonies are E.coli

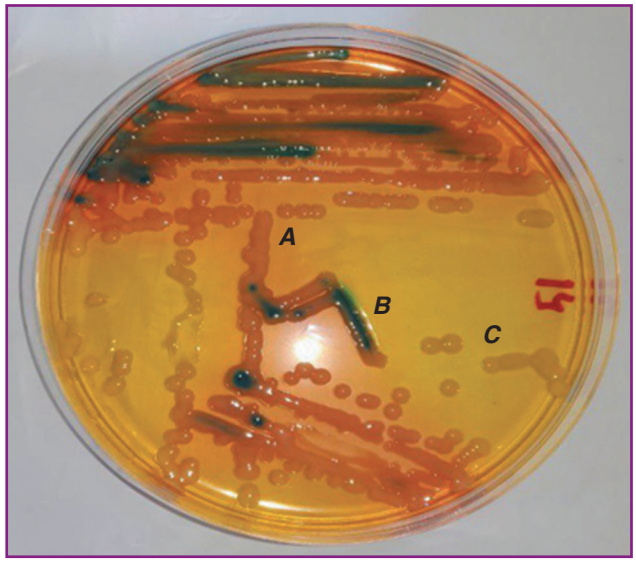

Figure 4. Lactobacillus spp.: A — L.acidophilus as pink colonies; B — green colonies are L.rhamnosus; C — yellow colonies represent L.fermentum

and decrease in the blood flow and elasticity [24]. Such alterations create a favorable microenvironment for dysbiosis. Additionally to, reduction in *Lactobacillus* spp., and this will rise the vaginal pH, resulting in growth of opportunistic microbes and uropathogens such as *E.faecalis*, *E.coli*, *S.aureus*, *C.albicans*, etc. that have role in existence of several urogenital symptoms includes vaginal dryness, burning, itching, irritation, and discharges [5]. These are most common manifestations in pot-menopausal women, and these chronic conditions expressed as GSM, which is another term of the vaginal atrophy [25–27].

Conclusions

Serum E2 and progesterone reach their highest levels during the reproductive years in pre-menopausal women but progressively decline from the peri-menopause stage, reaching baseline levels in post-menopause. FSH remains low during reproductive years but steadily increases as menopause progresses. Testosterone levels show minimal variation across menopausal stages. Additionally, *Lactobacillus* spp., particularly *L.acidophilus*, are more predominant in pre-menopausal women but significantly decrease in menopausal individuals. Conversely, opportunistic pathogens such as *E.faecalis*, *E.coli*, *S.aureus*, and *C.albicans* are more frequently isolated from menopausal women. The observed microbial dysbiosis and diversity in menopause and post-menopause are directly correlated with declining estradiol-2 and progesterone levels. Finally, a significant association was found between urogenital symptoms linked to GSM and the presence of pathogenic bacterial growth, reinforcing the critical role of hormonal and microbiome alterations in GSM severity.

References

1. *Talaulikar V. Menopause transition: Physiology and symptoms. Best Pract Res Clin Obstet Gynaecol. 2022 May;81:3-7. doi: 10.1016/j.bpobgyn.2022.03.003.*
2. *Harlow SD, Gass M, Hall JE, et al.; STRAW+10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. Climacteric. 2012 Apr;15(2):105-114. doi: 10.3109/13697137.2011.650656.*
3. *AlSwayied G, Frost R, Hamilton FL. Menopause knowledge, attitudes and experiences of women in Saudi Arabia: a qualitative study. BMC Womens Health. 2024 Nov 25;24(1):624. doi: 10.1186/s12905-024-03456-7.*
4. *Tariq B, Phillips S, Biswakarma R, Talaulikar V, Harper JC. Women's knowledge and attitudes to the menopause: a comparison of women over 40 who were in the perimenopause, post menopause and those not in the peri or post menopause. BMC Womens Health. 2023 Aug 30;23(1):460. doi: 10.1186/s12905-023-02424-x.*
5. *Angelou K, Grigoriadis T, Diakosavvas M, Zacharakis D, Athanasiou S. The Genitourinary Syndrome of Menopause: An Overview of the Recent Data. Cureus. 2020 Apr 8;12(4):e7586. doi: 10.7759/cureus.7586.*
6. *Qi W, Li H, Wang C, et al. The effect of pathophysiological changes in the vaginal milieu on the signs and symptoms of genitourinary syndrome of menopause (GSM). Menopause. 2020 Aug 17;28(1):102-108. doi: 10.1097/GME.0000000000001644.*
7. *Kumar L, Dwivedi M, Jain N, et al. The Female Reproductive Tract Microbiota: Friends and Foe. Life (Basel). 2023 Jun 1;13(6):1313. doi: 10.3390/life13061313.*
8. *Chee WJY, Chew SY, Than LTL. Vaginal microbiota and the potential of Lactobacillus derivatives in maintaining vaginal health. Microb Cell Fact. 2020 Nov 7;19(1):203. doi: 10.1186/s12934-020-01464-4.*
9. *Thomas-White KJ, Gao X, Lin H, et al. Urinary microbes and postoperative urinary tract infection risk in urogynecologic surgical patients. Int Urogynecol J. 2018 Dec;29(12):1797-1805. doi: 10.1007/s00192-018-3767-3.*
10. *Gajer P, Brotman RM, Bai G, et al. Temporal dynamics of the human vaginal microbiota. Sci Transl Med. 2012 May 2;4(132):132ra52. doi: 10.1126/scitranslmed.3003605.*
11. *Malik R, Pokeria C, Singh S. Correlation of Menopausal Symptoms with Serum Estradiol: A Study in Urban Indian Postmenopausal Women. J Obstet Gynaecol India. 2022 Aug;72(4):322-329. doi: 10.1007/s13224-021-01518-6.*
12. *Naji HH, Al-Watify DGU. The effects of Estradiol Deficiency on the Level of Lipids and Proteins of Postmenopause Women. Journal of Babylon University for Pure and Applied Sciences. 2017;25(2):421-434.*
13. *Naji HH, Al-Watify DGU. The effects of Estradiol Deficiency on the Level of Lipids and Proteins of Postmenopause Women. Journal of Babylon University: Journal of Applied and Pure Sciences. 2017;25(2):421-434.*
14. *Naji WA, Waheeb MQ, Aziz HA. Polyovarian cyst in women: a narrative review problem to mysterious progress. Biochemical and Cellular Archives. 2020;20(Suppl 2):3219-3205.*
15. *Mesen TB, Young SL. Progesterone and the luteal phase: a requisite to reproduction. Obstet Gynecol Clin North Am. 2015 Mar;42(1):135-151. doi: 10.1016/j.ogc.2014.10.003.*
16. *Regidor PA. Progesterone in Peri- and Postmenopause: A Review. Geburtshilfe Frauenheilkd. 2014 Nov;74(11):995-1002. doi: 10.1055/s-0034-1383297.*
17. *Practice Committee of the American Society for Reproductive Medicine. Testing and interpreting measures of ovarian reserve: a committee opinion. Fertil Steril. 2020 Dec;114(6):1151-1157. doi: 10.1016/j.fertnstert.2020.09.134.*
18. *Santoro N, Crawford SL, El Khoudary SR, et al. Menstrual Cycle Hormone Changes in Women Traversing Menopause: Study of Women's Health Across the Nation. J Clin Endocrinol Metab. 2017 Jul 1;102(7):2218-2229. doi: 10.1210/jc.2016-4017.*
19. *Handelsman DJ, Sikaris K, Ly LP. Estimating age-specific trends in circulating testosterone and sex hormone-binding globulin in males and females across the lifespan. Ann Clin Biochem. 2016 May;53(3):377-384. doi: 10.1177/0004563215610589.*
20. *Onderdonk AB, Delaney ML, Fichorova RN. The Human Microbiome during Bacterial Vaginosis. Clin Microbiol Rev. 2016 Apr;29(2):223-238. doi: 10.1128/CMR.00075-15.*
21. *Georges M, Odoyo E, Matano D, et al. Determination of Enterococcus faecalis and Enterococcus faecium Antimicrobial Resistance and Virulence Factors and Their Association with Clinical and Demographic Factors in Kenya. J Pathog. 2022 Nov 9;2022:3129439. doi: 10.1155/2022/3129439.*
22. *El Zowalaty ME, Lamichhane B, Falgenhauer L, et al. Antimicrobial resistance and whole genome sequencing of novel sequence types of Enterococcus faecalis, Enterococcus faecium, and Enterococ-*

cus durans isolated from livestock. Sci Rep. 2023 Oct 30;13(1):18609. doi: 10.1038/s41598-023-42838-z.

23. Engelsöy U, Svensson MA, Demirel I. Estradiol Alters the Virulence Traits of Uropathogenic Escherichia coli. Front Microbiol. 2021 Jul 20;12:682626. doi: 10.3389/fmicb.2021.682626.

24. Lakshmi K, Chitralekha S, Illamani V, Menezes GA. Prevalence of bacterial vaginal infections in pre and postmenopausal women. Int J Pharm Bio Sci. 2012 Oct-Dec;3(4):B949-B956.

25. Cucinella L, Tiranini L, Cassani C, et al. Insights into the vulvar component of the genitourinary syndrome of menopause (GSM). Maturitas. 2024 Aug;186:108006. doi: 10.1016/j.maturitas.2024.108006.

26. Shifren JL. Genitourinary Syndrome of Menopause. Clin Obstet Gynecol. 2018 Sep;61(3):508-516. doi: 10.1097/GRF.0000000000000380.

27. Azeez DA. Antifungal Activity of Mixture Eugenia Aromaticum and Thymus Vulgaris Essential Oils against Candida Albicans Clinical Strains in Al-Muthanna Province, Iraq. Plant Archives. 2020;20(1):172-174.

28. Makki MA, Azeez DA. Studying the level of hospital contamination with Staphylococcus aureus. Ro J Infect Dis. 2023;26(4):154-158. doi: 10.37897/RJID.2023.4.5.

Received 30.04.2025
Revised 10.06.2025
Accepted 22.06.2025

Information about authors
Hawraa Nasser Hamza, College of Science, Al-Muthanna University, Samawa, Iraq
Hanaa Ali Aziz, College of Science, Al-Muthanna University, Samawa, Iraq; e-mail: Hanabio-1983@mu.edu.iq; https://orcid.org/0000-0001-8173-5321
Dhay Ali Azeez, College of Science, Al-Muthanna University, Samawa, Iraq; https://orcid.org/0000-0002-4142-9298

Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Hawraa Nasser Hamza, Hanaa Ali Aziz, Dhay Ali Azeez
College of Science, Al-Muthanna University, Samawa, Iraq

Фізіологічні та мікробіомні взаємодії в патогенезі генітоуринарного менопаузального синдрому на різних етапах менопаузи

Резюме. Актуальність. Менопауза — це природний процес зниження функції яєчників, що призводить до зменшення рівня естрогену й прогестерону. Вона має три стадії: перименопауза, менопауза та постменопауза. Естроген відіграє ключову роль у підтриманні цілісності й мікробного балансу вагінального середовища. Фізіологічні та мікробіомні зміни впродовж стадій менопаузи впливають на тяжкість генітоуринарного менопаузального синдрому (ГМС), який включає комплекс симптомів, що уражають вагіну, сечовий міхур та уретру. **Мета:** дослідити кореляцію між коливаннями рівнів статевих гормонів і змінами у вагінальному мікробіомі, а також їхній вплив на тяжкість ГМС. **Матеріали та методи.** Дослідження тривало з вересня по грудень 2024 року. У ньому взяли участь 100 осіб: 75 жінок старше 45 років, які не мали менструацій протягом різних проміжків часу, та 25 жінок віком до 40 років із регулярним менструальним циклом. Клінічне обстеження проводили перед отриманням зразка. Для вимірювання концентрації гормонів використовували імуноферментний аналізатор BIOT-YG-I FIA, для ідентифікації мікробних ізолятів — середовища CHROMagar. **Результати.** Виявлено значну різницю в рівні естрадіолу-2: у жінок у пременопаузі він становив 179,17 ± 14,21, у перименопаузі — 64,72 ± 8,53, у менопаузі — 28,75 ± 3,49, у постменопаузі — 24,50 ± 2,46. Уміст прогестерону дорівнював 0,65 ± 0,06 у групі пременопаузи, 0,370 ± 0,018 — перименопаузи, 0,34 ± 0,017 — менопаузи та 0,304 ± 0,017 — постменопаузи. Середній рівень фолікулостимулюючого гормону був нижчим в учасниць у пременопаузі — 5,22 ± 0,90 проти 79,00 ± 7,49 у перименопаузі, 89,72 ± 8,70 у менопаузі та 94,17 ± 9,77 у жінок у постменопаузі. Середній рівень тестостерону був вищим у групі пременопаузи та становив 0,63 ± 0,06 порівняно з 0,480 ± 0,089 в учасниць у перименопаузі, 0,480 ± 0,078 — у менопаузі, 0,610 ± 0,091 — у постменопаузі. Частка *L.acidophilus*, виділеної зі зразка вагінального мазка, дорівнювала 12,0 % в групі перименопаузи, 16,0 % — менопаузи, 24,0 % — постменопаузи й 52,0 % — пременопаузи. Крім того, найчастіше ізольованим бактеріальним патогеном був *E.faecalis*: показник становив 64,0 % для учасниць у перименопаузі, 56,0 % — у менопаузі та 60,0 % — постменопаузі порівняно з 12,0 % в групі пременопаузи. У групах менопаузи й постменопаузи спостерігався значний зв'язок між урогенітальними симптомами та ростом бактерій (P > 0,05). **Висновки.** Рівні естрадіолу-2 та прогестерону поступово знижуються від перименопаузи до постменопаузи. Бактеріальна різноманітність переважає в жінок у постменопаузі. Також у постменопаузальній групі виявлено значну кореляцію між колонізацією бактеріями й урогенітальними симптомами, що підтверджує зв'язок між зміненим вагінальним мікробіомом і тяжкістю ГМС.

Ключові слова: статеві гормони; менопауза; генітоуринарний менопаузальний синдром; *Lactobacillus*; *E.faecalis*