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Review

Genitourinary syndrome of lactation: a new perspective on postpartum and lactation-related genitourinary symptoms

Sara Perelmuter, MPhil[1,*], Ramzy Burns, MD[2], Katie Shearer, BS[3], Raeven Grant, BS[4], Anantha Soogoor, BSc[5], Soyoun Jun, BSc[6], Janine Alexis Meurer, BS[7], Jill Krapf, MD[8], Rachel Rubin, MD[9]

[1]Weill Cornell Medical College, New York, NY 10021, United States
[2]Department of Urology, Indiana University, Indianapolis, IN 47405, United States
[3]University of Tennessee Health Science Center, Memphis, TN 38163, United States
[4]David Geffen School of Medicine, University of California, Los Angeles, CA 90095, United States
[5]College of Osteopathic Medicine, William Carey University, Hattiesburg, MS 39401, United States
[6]Texas College of Osteopathic Medicine, University of North Texas Health Science Center, Fort Worth, TX 76107, United States
[7]Jacobs School of Medicine and Biomedical Sciences, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, NY 14203, United States
[8]Obstetrics and Gynecology, Center for Vulvovaginal Disorders, Washington, DC 20037, United States
[9]Department of Urology, Georgetown University, Washington, DC 20007, United States

*Corresponding author: Weill Cornell Medical College, New York, NY 10021, United States. Email: sap4034@med.cornell.edu

Abstract

Background: The genitourinary syndrome of menopause (GSM) is a well-documented condition characterized by a range of genitourinary symptoms in peri- and postmenopausal women. As with GSM, postpartum lactating women experience reduced estrogen and androgen levels. However, there is limited research on the impact of symptoms during the postpartum breastfeeding period.
Objectives: The aim was to review the literature for genitourinary health in the postpartum breastfeeding population and summarize key findings and potential treatments.
Methods: We performed a comprehensive literature review in PubMed, Google Scholar, and Scopus from inception of database to November 2023 using the following keywords individually and in combination: "physiology of postpartum" or "physiology of lactogenesis" or "vulvovaginal health" or "vaginal atrophy" or "vaginal dryness" or "dyspareunia" or "urinary incontinence" or "lactation" or "breastfeeding" or "vaginal estrogen." All identified articles published in English were considered. Relevant studies were extracted, evaluated, and analyzed. The work presented in this article represents a summative review of the identified literature.
Results: During lactation, high levels of prolactin inhibit estrogen and androgen secretion via negative feedback, which leads to an increased prevalence of vulvovaginal atrophy, vaginal dryness, dyspareunia, and urinary incontinence in lactating postpartum women. Despite these highly prevalent and potentially devastating symptoms, there is a lack of consistent screening at postpartum visits and no treatment guidelines available to health care providers.
Conclusion: Postpartum breastfeeding women experience similar physiology and symptoms to the postmenopausal phase, as seen in GSM. We propose the introduction of a novel term to describe the genitourinary changes seen in postpartum breastfeeding individuals: genitourinary syndrome of lactation. The diagnostic use of genitourinary syndrome of lactation will equip health care providers with an all-encompassing term to bring awareness to the symptoms experienced by postpartum breastfeeding individuals and lead to improved screening and treatment for the high numbers of individuals experiencing these genitourinary changes.

Keywords: breastfeeding; lactation; postpartum; sexual health; vaginal atrophy; vaginal dryness; dyspareunia; genitourinary syndrome of menopause (GSM).

Introduction to genitourinary syndrome of lactation

Postpartum women during their lactation period experience a spectrum of genitourinary symptoms that often go overlooked. We propose the coining of a novel term—genitourinary syndrome of lactation (GSL)—to bring recognition to this multifaceted collection of genitourinary symptoms experienced by these women. This syndrome manifests through a variety of discomforts, including vaginal dryness, dyspareunia, urinary symptoms, and even alterations in sexual function, resulting in a significant impact on quality of life for affected individuals. GSL arises due to the intricate interplay between hormonal changes associated with lactation and physiologic alterations in the genitourinary tract. Despite its prevalence and the substantial implications that it carries for maternal well-being, GSL tends to be underrecognized in clinical settings, leading to underdiagnosis and inadequate management. Understanding the intricacies of GSL is crucial not only for health care providers but also for empowering women with knowledge about this condition, thereby enabling improved recognition, management, and support during the postpartum period. This review aims to comprehensively explore GSL, encompassing its pathophysiology, clinical manifestations, diagnosis, management strategies, and the broader impact that it has on the overall health and quality of life of lactating women.

Methods

Data were obtained by conducting a comprehensive literature search in PubMed, Google Scholar, and Scopus to identify

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relevant articles published from inception of database to November 2023. Databases were searched by a combination of controlled vocabulary and free text terms for vulvovaginal health and breastfeeding. Search keywords included "lactation," "lactogenesis," "physiology of postpartum," "vaginal dryness," "dyspareunia," "vaginal hormones," "breastfeeding," "postpartum," "vaginal health," "vulvovaginal atrophy," "sexual health," and "genitourinary syndrome." The search was not limited by publication type or year. We performed a comprehensive literature review of original research articles, meta-analyses, review articles, and consensus guidelines regarding the sexual health effects of breastfeeding. Additional articles were retrieved among references of the included studies or obtained via dedicated queries with less strict criteria aimed to investigate in more detail those strategies for which we found preliminary evidence. All identified articles published in English were considered. Relevant studies were extracted, evaluated, and analyzed. The work presented in this article represents a summative review of the identified literature.

Physiology of lactation and its impact on the genitourinary system

Lactation-induced hormonal shifts

Pregnancy progresses through distinct stages that affect breast development and lactation. In the first trimester, estrogen drives changes such as areola enlargement and type 3 lobule maturation, influenced by chorionic gonadotropin.[1] The second trimester sees increased progesterone leading to lobule proliferation and colostrum production with unique components crucial for infant immunity.[1,2] By the third trimester, mature secretory cells form, ready for colostrum production aided by oxytocin.[1] Postdelivery, lactation enters stage II, marked by a drop in progesterone and a rise in prolactin triggering milk buildup in the alveoli and ducts.[2] Elevated prolactin results in decreased ovarian production of androgens and estrogens. The mechanism behind this phenomenon can be elucidated by understanding how hyperprolactinemia leads to the inhibition of hypothalamic Kiss1 neurons, which play a direct role in regulating the pulsatile release of gonadotropin-releasing hormone (GnRH). Kisspeptin, a neuropeptide, has been identified as the most powerful stimulator of GnRH secretion,[3,4] where mutations in either the *Kiss1* gene or the *Kiss1* receptor gene have been associated with idiopathic hypothalamic hypogonadism and reduced luteinizing hormone pulse amplitudes in humans,[4,5] highlighting the pivotal role of kisspeptin in the proper functioning of the hypothalamus-pituitary-ovarian axis. Research in female mice has demonstrated that the infusion of prolactin leads to the suppression of ovarian function through the inhibition of GnRH and *Kiss1* mRNA expression, where administration of kisspeptin restores normal ovarian function.[6] It is important to emphasize that while estrogen and progesterone are required for the development of the mammary glands and during the final months of pregnancy, levels of estrogen and progesterone fall at delivery, allowing prolactin to increase and initiate milk production.[7] Following this initiation, the maintenance of lactation depends on prolactin, which in turn suppresses estrogen and androgen release.[2]

While the exact mechanisms governing alterations in the hypothalamus-pituitary-ovarian axis during lactation are still not fully understood, we can provide a broad overview of the events that lead to the postpartum lactating hypoestrogenic state. Suckling remains the primary stimulus for maintaining

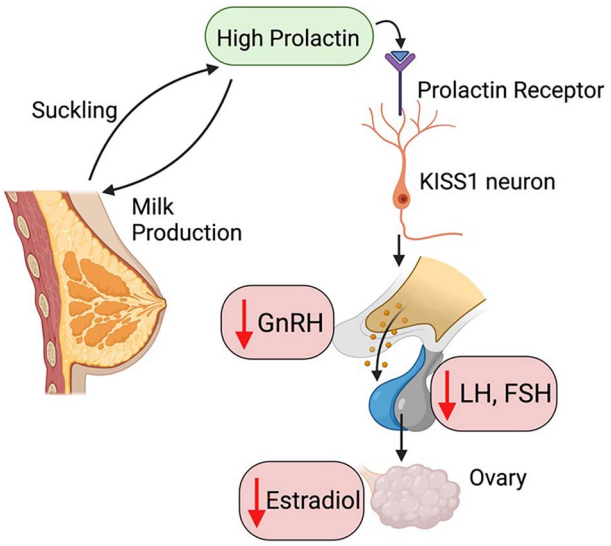

Figure 1. Lactation-induced hormonal shifts elevate prolactin, resulting in decreased ovarian production of androgens and estrogen. As a consequence, the lactating woman experiences a hypoestrogenic and hypoandrogenic state, which may persist as long as lactation is continued. Prolactin suppresses gonadotropin-releasing hormone and gonadotropin, which in turn blocks folliculogenesis and aromatase enzymes. This further potentiates a hypoestrogenic state.

the suppressive effect on the ovaries after pregnancy. Breastfeeding results in elevated levels of prolactin, which persist at higher-than-normal levels until the frequency and duration of daily suckling decrease sufficiently to reset the hypothalamus-pituitary-ovarian axis. Hyperprolactinemia triggers the suppression of hypothalamic Kiss1 neurons, which directly regulate the pulsatile release of GnRH. This disruption in the pulsatile pattern of GnRH secretion leads to a significant decrease in the frequency of corresponding luteinizing hormone pulses. Insufficient luteinizing hormone and follicle-stimulating hormone secretion ultimately result in a reduced estrogens and androgens state (Figure 1).

As a result, the lactating woman experiences a hypoestrogenic and hypoandrogenic state, which may persist as long as lactation is continued. Lactation decreases the risk of further pregnancy, which from an evolutionary standpoint could disrupt the infant's care. Prolactin suppresses GnRH and gonadotropin, which in turn blocks folliculogenesis and aromatase enzymes. This further potentiates a hypoestrogenic state, similar to menopause.[8] For example, while the duration of lactational amenorrhea varies significantly, a multicenter study involving 8 countries revealed that 65% to 70% of breastfeeding women continued to experience amenorrhea 7 months after childbirth.[9] This illustrates the significant impact and commonality of the postpartum hypoestrogenic state.

Effects of hormonal shifts on the genitourinary system

Estrogen plays a critical role in maintaining vaginal wall thickness and lubrication, as well as urethral and vulvar thickness.[10] The estrogen receptors themselves are located throughout the female genitourinary tract, including the clitoris, bladder trigone, urethra, and vulvovaginal epithelium.[11] Additionally, estrogen is suggested to be responsible for maintaining high levels of *Lactobacillus* species by maintaining glycogen

levels,[12,13] where lactobacillus colonization is a primary factor that maintains a healthy acidic vaginal pH. Decreased estrogen levels during lactation can lead to decreased vaginal lubrication, dyspareunia, incontinence, and vulvovaginal atrophy.[14]

Androgens work synergistically with estrogen to maintain the vascularity of vaginal tissue. Androgen receptors are abundant in the dermis of the labia minor and vestibule and have been repeatedly detected throughout the genitourinary tract via Western blot, immunohistochemistry, ligand binding, and gene expression.[15,16] This allows vascular congestion to build up so that transudate can flow through the epithelium and lubricate the vaginal walls.[17] Conversely, progestins inhibit smooth muscle cell growth, thus inhibiting vasodilation and lubrication.[17] Progesterone is a significant negative predictor of sexual desire and ability to lubricate.[18]

As such, decreased androgens and estrogens contribute to superficial dyspareunia and vestibulodynia and can limit sexual desire.[14,16,19] Multiple mechanisms involved have been postulated, with a lack of unanimous results. Hormones may affect the vestibular epithelium through interaction with their hormone receptors or via alteration of receptor expression.[20-22] Additionally, estrogen and progesterone may act as endogenous pain modulators; the direct effect of progesterone on unmyelinated sensory nociceptor neurons has been described.[23,24] Overall, the effect of hormones is likely multifactorial.

Clinical manifestations

Overview of symptoms associated with GSL

Vulvovaginal atrophy

Few studies have investigated postpartum women and the breastfeeding-related hypoestrogenic/hypoandrogenic state in relation to vulvovaginal atrophy and dyspareunia. Of the literature that does exist, Lev-Sagie et al found that vulvovaginal atrophy was significantly more common in breastfeeding women as compared with nonbreastfeeding women, consistent across 3 criteria: gynecologic examination (57.6% vs 16.7%), pH (70% vs 22%), and, most markedly, cytologic evaluation by vaginal maturation index (VMI; 51.1% vs 0%).[25] Despite diagnosis via these different means, this study revealed that vaginal atrophy was consistently prevalent in the lactating population.[25]

In another study, Wisniewski and Wilkinson noted lactation as a potential causal factor for postpartum vaginal atrophy.[26] The authors reported that 67.6% of breastfeeding mothers had vaginal atrophy, as opposed to only 32.4% of nonbreastfeeding mothers.[26] The authors concluded that the comparison of control and atrophy by the presence of lactation indicates a statistically significant correlation ($P < .0001$) between vaginal atrophy and breastfeeding. However, they noted that this relationship was not universal and was likely a result of variations in estrogen receptors and peripheral conversion of androstenedione to estrone in adipose tissue.[26]

Vaginal dryness

The hormonal changes associated with lactation have been consistently linked to the occurrence of vaginal dryness, historically[27,28] and currently.[14,29] One study revealed that breastfeeding women were more likely to report vaginal dryness than those who did not breastfeed at 3 weeks (13.3% vs 3.8%) and 6 weeks (17.5% vs 2.3%).[10] Other studies measuring self-reported sexual behavior and sexual dysfunction also noted that vaginal dryness was a consistent and primary concern.[30] This induced vaginal dryness can cause discomfort, irritation, and pain during sexual intercourse, affecting the quality of life for breastfeeding individuals. While vaginal dryness is a common side effect of lactation-related hormonal changes, there has been minimal attention, screening, or attempted management in the postpartum lactating population.[30]

Dyspareunia

In addition to vulvovaginal atrophy and vaginal dryness, postpartum dyspareunia was more frequently observed in breastfeeding women (80%) vs nonbreastfeeding (50%). Masters and Johnson—the pioneers of human sexual response research—published observations comparing visual examinations of breastfeeding and nonbreastfeeding mothers at 4, 8, and 12 weeks postpartum.[31] They reported flattened rugal patterns and a "senile"-appearing light pink color change, and they noted that nursing patients had a "steroid starvation pattern." Interviews at 12 weeks with 101 participants showed that 10.9% cited vaginal tightness and 46.5% vaginal irritation or dyspareunia.[31]

However, overall literature is inconclusive regarding the association between breastfeeding and dyspareunia. While multiple studies have identified breastfeeding as a risk factor for dyspareunia at the time of initial sexual intercourse postpartum, 3 months postpartum,[30,32] and 6 months postpartum,[30,32,33] another study did not find this association.[34] This disparity may be due to varying sample sizes and the lack of standardized characterization of the frequency and severity of pain, as well as to diverse hormonal and physiologic changes at different points in the postpartum period.

Additionally, the study and diagnosis of dyspareunia and female sexual dysfunction necessitate a biopsychosocial approach. In the setting of the postpartum period, sexuality can be complicated by new psychological stressors, health complications sustained in the peripartum period, and physiologic changes that come with breastfeeding and postpartum recovery.

It is also important to note the potential causes of dyspareunia: perineal trauma from vaginal delivery, poor wound healing of episiotomy, or spontaneous perineal laceration repairs. Of the scarce literature that is available on breastfeeding and vulvovaginal health, there are clinical implications regarding recovery from the physical birth and any tissue trauma experienced. Comparison between vaginal and cesarean deliveries revealed no difference in the prevalence of postpartum dyspareunia,[35,36] and mechanical trauma was not a statistically significant factor in vaginal atrophy.[26] However, studies have found that dyspareunia at 6 months postpartum, while not associated with type of delivery, was significantly associated with current breastfeeding.[30]

Impact of lactation on vulvovaginal healing

The lack of estrogen in the postpartum lactating state may impede recovery from vulvovaginal tears after vaginal delivery. While the mode of delivery itself has not been correlated to significant differences in vaginal atrophy, the lack of estrogen and androgens in the postpartum breastfeeding state may play an impeding role in recovery. More than 85% of vaginal

births result in some degree of trauma.[37] Risk factors for severe perineal trauma include primary vaginal delivery, large or malpositioned baby, advanced maternal age, abnormal collagen synthesis, and/or forceps delivery.

Estrogen promotes the growth of keratinocytes and enhances re-epithelialization such that a reduction in estrogen levels leads to a decrease in wound collagen.[38] Impaired healing resulting from estrogen deficiency is associated with decreased expression of growth factors, reduced keratinocyte growth, and synthesis of wound proteases, all of which contribute to delayed re-epithelialization.[39] Studies have demonstrated that supplementation of estrogen can reverse the breakdown of the extracellular matrix by inhibiting wound protease synthesis and can boost the formation of collagen during the wound repair phase.[40,41] In fact, research has shown that postmenopausal women treated with hormone therapy experienced levels of matrix collagen deposition and a rate of wound re-epithelialization similar to premenopausal women, while those not undergoing hormone therapy showed reduced collagen formation and re-epithelialization in the extracellular matrix.[40,41] These improvements seen with estrogen supplementation were attributed to an increase in the proliferation of epidermal keratinocytes.

Taken together, it would be plausible that lactating women, who are thus in a hypoestrogenic state, may have delayed or impeded recovery as compared with postpartum women who are not breastfeeding. To our knowledge, there have been no studies investigating this potential relationship.

Postpartum urinary incontinence

Postpartum urinary incontinence (UI) is a significant but frequently underestimated aspect of maternal health problems. The reported average incidence of UI at 1 year postpartum is 31%, with a range of 10% to 63%.[42] Stress UI (SUI) is the most prevalent type at 54% 1 year postpartum,[42] making this condition an extremely common finding. Additionally, UI can be emotionally distressing and shameful for women, leading to a decrease in their overall quality of life.[43] Numerous clinical investigations have aimed to pinpoint the specific obstetric events responsible for causing incontinence. Potential culprits include the delivery of large infants and challenging childbirths characterized by a prolonged second stage of labor, with or without the use of operative vaginal delivery with forceps or vacuum. However, no singular event has been definitively linked to the condition, indicating that postpartum UI likely results from a complex combination of physiologic factors. The ramifications of this underlying physiology extend beyond urinary leakage, pelvic organ prolapse (including cystocele, rectocele, and uterine prolapse), and anal incontinence, all of which can be extremely distressing. Yet, these prevalent pelvic problems receive scant attention.

Interestingly, the association between SUI and collagen is well established: the expression levels of type I and III collagen are significantly lower in patients with SUI when compared with a control group ($P < .01$).[44] Correspondingly, in more recent investigations, a prospective study assessing SUI symptoms before and after topical estriol therapy found improvement on the Urogenital Distress Inventory stress domain after 6 weeks of treatment,[45] and another study similarly found a significantly improved change in SUI outcome measures after 12 weeks of vaginal estriol cream in postmenopausal women with stress incontinence.[46] It is important to underscore that the estrogen used in these 2 studies is estriol, as estrogen administration is not currently available in the United States. Taken together, these data suggest that because estrogen supplementation improves UI symptoms, the lack of estrogen may contribute to the origin of UI. As such, individuals with decreased estrogen levels may be more susceptible to UI symptoms, such as the postpartum lactating population.

However, there exists a gap of literature and data on the effect of the postpartum breastfeeding hypoestrogenic state on UI. Namely, do women who breastfeed have prolonged UI as compared with postpartum women who do not breastfeed? We propose that breastfeeding women may experience UI and other urinary symptoms similar to those experienced in the genitourinary syndrome of menopause. There is a need for future research to investigate postpartum UI and lactation.

Tools for GSL assessment

Examination and patient interaction

Assessing vulvovaginal health in lactating individuals often involves visual examination of the vulva, vulvar vestibule (including the urethral meatus), and vaginal mucosa. Examination of the vulva and vulvar vestibule should be aided by lighting and microscopy via a vulvoscope. Examination of the vagina may be done during a speculum examination, ideally with the aid of saline microscopy and pH evaluation of vaginal discharge. Pelvic organ prolapse can also be evaluated at the time of pelvic examination. During a gynecologic examination, clinicians can observe various indicators in the vulva, vestibule, and vagina, such as epithelial thinning, erythema, pallor, dryness, loss of rugation, petechiae, friability, and tenderness. This can be paired with the visual analog scale, where the patient rates her pain with a handwritten mark placed at one point along a 10-cm line, which represents a continuum between the ends of the scale (no pain, 0 cm; worst pain, 10 cm). Additionally, standardized questionnaires such as the Female Sexual Function Index are used to assess sexual dysfunction. However, there is no universally accepted standard for routinely evaluating genitourinary changes in postpartum lactating women. This absence of standardized screening contributes to the underdiagnosis of these changes, thereby hindering the implementation of appropriate treatment measures.

Vaginal microbiome and pH

One established method for assessing vulvovaginal atrophy involves measuring vaginal pH. The presence of *Lactobacillus* bacteria and glycogen metabolism within epithelial cells leads to the production of lactic acid, resulting in an acidic vaginal environment.[47] An analysis of vaginal pH can be utilized as a measure of vaginal health. Specifically, vaginal pH measurements ≤ 4.5 are optimal, while ≥ 5 may be a marker of vulvovaginal atrophy, desquamative inflammatory vaginitis, or bacterial vaginosis.[48] Furthermore, using pH as a means of diagnosis rather than clinical-based diagnosis can improve sensitivity.[25]

Vaginal maturation index

The VMI is a method to evaluate vaginal health through cytologic assessment.[49] A vaginal sample taken by a cotton swab from the middle of the vagina is stained with hematoxylin and eosin on a glass slide for analysis. Mature squamous epithelial cells are assigned a value of 1.0, intermediate cells 0.5, and parabasal cells 0, with the total calculated by multiplying the

cell counts by their respective values and dividing by the total number of cells. VMI values from 0 to 49 indicate atrophy due to low estrogen levels; 50 to 64, mild atrophy; and 65 to 100, a healthy vaginal state with high estrogen levels. Low vaginal pH aligns with high VMI values, validating different diagnostic techniques. However, symptom presentation does not consistently align with VMI or physical examination, emphasizing the limitation of using symptoms alone for diagnosis. VMI is typically done in the research setting and not often clinically. Notably, women undergoing estrogen therapy exhibit higher VMI values, suggesting the potential effectiveness of interventions such as vaginal estrogen therapy for vaginal health.

Vaginal health index

The vaginal health index serves as a widely employed clinical tool to evaluate vulvovaginal atrophy, assessing 5 key aspects: vaginal flexibility, discharge, pH levels, mucous membrane condition, and moisture. The overall extent of atrophy is gauged by tallying scores from each parameter, resulting in a total score ranging between 5 and 25. A score <15 signals the presence of vulvovaginal atrophy, guiding diagnosis based on these specific criteria.[50]

Transabdominal sonography

A recent pilot study introduced the idea of measuring vaginal wall and total vaginal mucosal thickness using transabdominal ultrasound around the bladder trigone, although this method has not been validated.[51] The study involved individuals aged 22 to 69 years and established a connection between vaginal wall thickness and menopausal status/vaginal atrophy. This approach might serve as a forthcoming tool to link thickness measurements with symptoms and treatment response for atrophy in the future.

Management and treatment approaches

Nonpharmacologic interventions for GSL

Given the similarities between the hormonal axis of a lactating female and a menopausal woman, many of the well-established treatment options for menopausal women can be utilized in women who are lactating. One of the most bothersome symptoms that women endorse is decreased vaginal lubrication. Therefore, vaginal lubricants and moisturizers are often considered a first-step approach for breastfeeding women with vaginal dryness and dyspareunia.[52,53]

A nonpharmacologic therapy that has demonstrated efficacious results in early studies on adverse genitourinary symptoms is vaginal hyaluronic acid (HA). A nonrandomized comparison cohort study found that 50 postmenopausal women using a vaginal get containing HA had significantly improved vulvovaginal atrophy, sexual function, and somatic aspects of quality of life after 12 weeks of treatment as compared with a control group using non-HA lubricants and moisturizers.[54] A larger multicenter open-label study based on a randomized controlled design compared the efficacy of HA and estriol cream to treat vaginal dryness in postmenopausal women, finding that HA and estriol cream significantly improved symptoms at rates of 84.44% and 89.42%, respectively.[55] Mechanistically, HA has been postulated to aid in the process of vaginal atrophy repair by facilitating sufficient vaginal hydration.[56]

Pelvic floor physical therapy (PFPT) has emerged as a beneficial intervention for lactating women experiencing various genitourinary postpartum challenges. By incorporating targeted exercises, manual techniques, and education on proper posture and body mechanics, PFPT aims to strengthen and restore pelvic floor muscle function, improve bladder and bowel control, enhance sexual well-being, and aid in overall postpartum recovery. This therapy offers a noninvasive and tailored approach, empowering lactating women to regain confidence and quality of life while managing the physical changes associated with childbirth and lactation. In a 2018 Cochrane review of 38 randomized controlled trials (RCTs), 6 RCTs of continent pregnant women compared patients who performed antenatal PFPT with those who did not, finding that the former had a lower risk of UI in late pregnancy and up to 6 months postpartum.[57] Likewise, a meta-analysis of 15 RCTs revealed that postpartum women receiving PFPT were less likely to report UI up to 12 months postpartum than those not receiving PFPT.[58] Pooling of data from 3 RCTs showed that women undergoing PFPT were less likely to report pelvic organ prolapse up to 12 months postpartum.[58] Furthermore, pooling of data from 4 RCTs showed a reduction in unsatisfactory sexual function up to 12 months postpartum for those who performed structured PFPT as compared with those who did not.[58] Taken together, the available evidence suggests that PFPT should be recommended during pregnancy and in the postpartum period to prevent, manage, and treat UI, pelvic organ prolapse, and postpartum sexual dysfunction. Further studies should investigate whether there is a difference in PFPT with local hormone therapy vs PFPT alone for the treatment of GSL.

Among nonpharmacologic treatment, fractional microablative CO_2 laser is being studied for vulvovaginal atrophy. In a multicentric retrospective study, 44 postpartum and/or breastfeeding women who were affected by persistent vaginal atrophy, chronic perineal pain, and deep dyspareunia were compared with a control group of 42 patients. The study evaluated the efficacy of CO_2 laser treatment on transient vulvovaginal atrophy and perineal pain related to the postpartum and breastfeeding period. The researchers reported a significant improvement for dyspareunia, pain at the vaginal orifice, and dryness.[59] Several studies have assessed the efficacy and feasibility of fractional CO_2 laser for the treatment of symptoms related to vulvovaginal atrophy in postmenopausal women, yielding positive results in terms of vulvovaginal atrophy symptoms (vaginal dryness, burning, itching, and dyspareunia), sexual function, and quality of life.[60,61] However, proper provider training to operate the laser is critical to avoid side effects and optimize laser performance, given that this is not a cosmetic or aesthetic treatment but a medical therapy to improve adverse symptoms.

Pharmacologic options and their efficacy

For breastfeeding women with refractory vaginal dryness or additional complaints of dyspareunia, recurrent UTIs, or significant vulvar and vaginal changes noted on examination, vaginal estrogen therapy can be considered. There are limited studies assessing the safety or efficacy of vaginal estrogen therapy in lactating women. One randomized placebo-controlled trial assessed vaginal estrogen cream applied twice weekly vs placebo for 12 weeks postdelivery.[62] There was no significant difference between the groups for the primary outcome, the Vulvar Assessment Score, or the secondary outcomes, which were quality-of-life and sexual function scores. The authors did, however, find excellent compliance with the

vaginal estrogen cream; from a subjective standpoint, 52% of participants reported that their perineum felt "very much better," as opposed to 31% in the placebo arm.[63] There were no serious adverse events noted in the study.

The concern with vaginal estrogen therapy in this population is that it may transfer to breast milk or cause decreased lactation. This was first studied in 1978 where 6 lactating women were given suppositories of vaginal estrogen (50-100 mg) and their serum and milk estradiol levels were measured.[64] Despite the high concentrations of vaginal estrogen administered (a standard regimen today is 10 mcg twice weekly), they found a serum:milk ratio <10:1. In another study, a transdermal estradiol patch (50, 75, or 100 mcg) was placed on breastfeeding women 20 weeks postpartum.[63] Even at the highest dose, there were no traces of measurable concentrations of estradiol detected in breast milk samples. An additional study corroborated these findings, with up to 200 mcg of transdermal estradiol administered to breastfeeding mothers. Again, there were no significant changes in infants' estradiol levels or growth patterns.

Another concern for postpartum mothers is the impact of estrogen therapy on breastmilk supply. Numerous studies have shown that there are no significant systemic changes in levels of estradiol when administered vaginally at low doses (10 mcg). Specifically, one such study showed that when women were administered a 7.5-mcg estradiol ring or 10-mcg estradiol tablet, plasma levels did increase above a postmenopausal level.[65] This is why the use of low-dose vaginal estrogen is considered safe, even in women with estrogen receptor–positive malignancies.[65] Given the lack of plasma estradiol changes, it is unlikely that there would be any effect on breast milk production.

Note that the doses of vaginal estrogen currently recommended and available are lower than the relatively high-dose estradiol suppositories utilized in older studies. Even so, the patient package insert included with low-dose vaginal estrogen therapies states, "Estrogen administration to nursing women has been shown to decrease the quantity and quality of the breast milk. Detectable amounts of estrogens have been identified in the breast milk of women receiving estrogen therapy." This statement is unsupported by current literature. Unfortunately, this strongly worded language may lead to fear in prescribing clinicians and lactating mothers.

Vaginal dehydroepiandrosterone

Vaginal dehydroepiandrosterone (DHEA), also known as prasterone, is indicated for the genitourinary syndrome of menopause and is Food and Drug Administration approved for treatment of moderate to severe dyspareunia in postmenopausal women. Vaginal DHEA works by cellular intracrinology, which converts DHEA to estrogen and testosterone on a cellular level; therefore, there is limited concern for systemic absorption. The human vagina is an androgen-target organ with the ability to synthesize androgens, thus providing support for the use of androgen for local genitourinary symptoms.[66] There are no studies of vaginal DHEA in the setting of lactation; as such, efficacy and safety in this setting are unknown. Vaginal DHEA is not currently used in lactating mothers due to the lack of studies in this population, despite the intracrinology mechanism.[67,68]

Future directions and research opportunities

Current gaps in understanding GSL

Two key factors contribute significantly to the challenge of diagnosing GSL. The first factor is the scarcity of research directly addressing the clinical manifestations of lactation alongside their underlying molecular mechanisms. The second factor is the absence of an established diagnosis and validated diagnostic criteria.

In summary, our review highlights the significant physiology of lactation and its impact on the genitourinary system. Lactation-induced hormonal shifts include elevated levels of prolactin that trigger suppression of hypothalamic Kiss1 neurons, leading to disruption of the pulsatile pattern of GnRH secretion. The downstream resulting decrease in luteinizing hormone and follicle-stimulating hormone secretion ultimately results in a hypoestrogenic state. Consequences of reduced estrogen and androgens include decreased vaginal lubrication, dyspareunia, incontinence, and vulvovaginal atrophy, as well as reduced vulvovaginal healing, which may be critical following vaginal delivery. While tools for assessing these clinical manifestations as well as treatment options exist, they are minimal and limited, as research focused on GSL is scarce. Taken together, it is imperative for these prevalent symptoms in the lactating postpartum population to be effectively addressed in clinical practice, and future research is needed to address these concerns.

In conclusion, our primary objective is to increase awareness surrounding the genitourinary changes and symptoms experienced by a significant proportion of lactating individuals. This endeavor is intended to catalyze heightened public consciousness, propel forthcoming research endeavors, and advance screening protocols. Additionally, the introduction of a novel diagnostic entity, GSL, is poised to facilitate accurate identification and diagnosis of these genitourinary alterations among lactating individuals. The introduction of the genitourinary syndrome of menopause provided an accurate and comprehensive description of a common symptomatic postmenopausal condition, which improved and increased communication, research, education, and treatment related to the genitourinary and sexual health of menopausal women.[69,70] We anticipate that introducing the novel term *genitourinary syndrome of lactation* will achieve the same results. GSL continues to be significantly underdiagnosed despite its widespread occurrence. This may be due to the reluctance of women to seek assistance, often driven by feelings of embarrassment, or the tendency among many women to consider these symptoms a "normal" aspect of the postpartum experience. Nevertheless, it is important to acknowledge that in numerous instances, health care providers' hesitance to address these concerns contributes significantly to the overall lack of awareness surrounding this syndrome among the affected female population. The introduction of the new term *genitourinary syndrome of lactation* not only elevates diagnostic precision but enhances our comprehension, management, and comprehensive treatment of the condition, ultimately benefiting health care providers and their patients.

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Conflicts of interest

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