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MINI-REVIEW

Vaginal microbiome: normalcy vs dysbiosis

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Abstract

It has been long understood that the vaginal microflora is crucial in maintaining a normal physiological environment for the host and its involvement is deemed indispensable for reproductive success. A global concept of normalcy vs. dysbiosis of vaginal microbiome is debatable as women of different races have a unique vaginal microflora with regional variations. Vaginal microflora is a dynamic microenvironment affected by gestational status, menstrual cycle, sexual activity, age, and contraceptive use. Normal vaginal flora is dominated by lactobacilli especially in women of European descent vs. African American women. These microbes confer the host vagina protection from potentially pathogenic microbes that may lead to urinary tract infections and sexually transmitted diseases. Changes in the vaginal microbiota including reduced lactobacilli abundance and increased facultative and anaerobic organism populations result in bacterial vaginosis, that predisposes the host to several conditions like low birth weight and increased risk of contracting bacterial infections. On the other hand, the vaginal microbiome is also reshaped during pregnancy, with less microbial diversity with a dominance of *Lactobacillus* species. However, an altered vaginal microbiota with low lactobacilli abundance especially during pregnancy may result in induction of excessive inflammation and pre-term labor. Since the vaginal microbiome plays an important role during embryo implantation, it is not surprising that bacterial vaginosis is more common in infertile women and associated with reduced rates of conception. Probiotic has great success in treating bacterial vaginosis and restoring the normal microbiome in recent. This report, reviewed the relationships between the vaginal microbiome and women's reproductive health.

Keywords Vaginal microbiome · Vaginal dysbiosis · Bacterial vaginosis · Pre-term birth · Infertility · *Lactobacillus*

Introduction

Microbiota plays a fundamental role in human physiological mechanisms, such as immunity and nutrition. They form a mutually beneficial relationship with the human host, where the host provides shelter and nutrition, and in return, they protect the host from a variety of pathogenic micro-organisms (Ursell et al. 2012). Microbiota act as a frontline defender against invading micro-organisms by a phenomenon termed 'colonization resistance', i.e. it prevents foreign organisms from colonizing the human body sites and consequently causing infection (Eckburg et al. 2005). The structure of the microbial communities in microbiota is crucial for the health status of an individual. Microbial dysbiosis impairs the health status by enhancing the susceptibility of the host to a spectrum of inflammatory and metabolic disorders like obesity and irritable bowel syndrome (Panda et al. 2014).

Dysbiosis in vaginal microbiota may be physiological or pathological depending on interplay of metabolic and microbial factors. Vaginal microbiota evolves with age, with anaerobic microbes being dominant in pre-pubertal age to the *Lactobacillus*-rich vagina in reproductive age (Ravel et al. 2011). The hormonal influence is also an important factor that determines the different phases of a women's reproductive cycle. Among hormones, estrogen is known to create distinctive changes in the vaginal microbiota (Farage

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et al. 2010). Physiologic (pregnancy and menstrual cycle) and pathologic changes (bacterial vaginosis, urinary tract infections, and sexually transmitted diseases) are associated with significant changes in the vaginal microbiota (Lamont et al. 2011).

Vaginal microbiota

Vaginal microbiota constitutes about 9% of the total human microbiota (Sirota et al. 2014). These microbes live in a mutualistic relationship with the host vagina protecting it from potentially pathogenic microbes like those causing bacterial vaginosis, urinary tract infections, candida infections, and sexually transmitted diseases (STDs) (Sobel 1999).

Vaginal microflora is a dynamic microenvironment where gestational status, use of contraceptives, menstrual cycle, and sexual activity contribute to variation in the bacterial communities (Gajer et al. 2012; DiGiulio et al. 2015; Huang et al. 2015). Conventionally normal vaginal flora has been thought to be dominated by lactobacilli (Hillier et al. 1993). Usually, *L. iners, L. crispatus, L. gasseri, and L. jensenii*, have been shown to predominate in the vaginal microbiota in healthy women of reproductive age in varied proportions (Martínez-Peña et al. 2013; Pendharkar et al. 2013; Drell et al. 2013). About 120 species of *Lactobacillus* have been documented and 20 are known to inhabit the vagina. The vaginal microbiota of healthy women comprises one or two lactobacilli species (Lamont et al. 2011; Jakobsson and Forsum 2007). However, recent advances in culture-independent approaches reveal the diversity and variability in the composition of a healthy vaginal microbiome. The healthy vaginal tract contains more than 50 non-pathogenic microbial species (Saunders et al. 2007; Oakley et al. 2008; Cribby et al. 2008). Bacterial clusters associated with ethnic groups have also been observed (Ravel et al. 2011; Drell et al. 2013). Surprisingly, several anaerobic bacteria were dominant, indicating that *Lactobacillus* dominance is not a necessary characteristic of healthy vaginal flora (Ravel et al. 2011). On the other hand, bacterial genera including *Prevotella*, *Atopobium*, *Gardnerella*, *Megasphaera*, and *Mobiluncus* have been associated with abnormal vaginal microbiota (Ravel et al. 2011; Drell et al. 2013) in asymptomatic reproductive-age women.

Ethnicity seems to be an important factor in determining the risk of bacterial vaginosis and is often linked to increased risk of PTB (Ravel et al. 2011; Harwich et al. 2012). Furthermore, reduced microbial diversity was also observed in the vaginal microbiome of pregnant women as pregnancy advanced, and greater vaginal microbial diversity were observed in mothers delivering on term compared with preterm births (Hyman et al. 2014; Aagaard et al. 2012; Romero et al. 2014a). Moreover, an abundance of *Lactobacillus* species in healthy pregnant women could be seen (Aagaard et al. 2012). Despite the relative stability of the vaginal microbiota of pregnant women, communities tend to shift from the dominance of one *Lactobacillus* species to another (Aagaard et al. 2012). Although the vaginal microbiome is variable, it is shown to have higher stability than other bodily habitats like the oral cavity, skin, and gut (Li et al. 2013).

Plasticity of the vaginal microbiota of young healthy women

Studies from around the globe have established the dominance of *Lactobacillus* species as the major component of vaginal microbiota in healthy women of reproductive age. However, ethnic, racial, regional, and species-level differences exist in vaginal microbiota. *Lactobacillus* species were first isolated and cultured from vaginal secretion by Doderlein in 1892. He published a monography 'Das Scheidensekret' (Vaginal secretions) in which he reported the presence of bacilli-shaped bacteria in the vagina termed Doderlein bacilli and later *Lactobacillus acidophilus* in 1928 (Lamont et al. 2011).

Lactobacillus in the vagina forms a finely tuned mutualistic relationship where they serve to protect vaginal mucosa from non-indigenous and foreign infectious particles. The potential abilities to prevent the colonization of pathogens or unwanted microbes are conferred by residential *Lactobacillus* species through the production of lactic acid. For instance, lactic acid acidifies the vaginal pH (3.5–4.5) and such low pH offers protection against viral (HIV), bacterial (*Neisseria gonorrhea*, and parasitic (*Trichomonas vaginalis*) agents (Martín et al. 2010; Vandenbergh 1993; Boris and Barbés 2000). *Lactobacillus* species in the vagina also produce antimicrobial substances called bacteriocins which are protein in nature and have a bactericidal effect on the growth of other bacteria (Karaoğlu et al. 2003). Some species of *Lactobacillus* are also known to produce hydrogen peroxide which also possesses antimicrobial activity, thus discouraging colonization of pathogenic organisms (Fig. 1). Studies have revealed that peroxide-producing species of *Lactobacillus* are more protective compared to non-producers (O'Hanlon et al. 2013) (Figs. 2 and 3).

Human Microbiome Project has brought the microbiome into the limelight in the arena of research. Scientists from all over the world have conducted studies in their respective regions to unveil the vaginal microbiome profiles. The concept of normalcy of vaginal microbiome is a bit controversial as women from different countries have an element of uniqueness in their vaginal microbiome with slight regional variations. According to Deborah et al., *L. crispatus*, *L. iners,* and *L. jensenii* are prevalent species in the

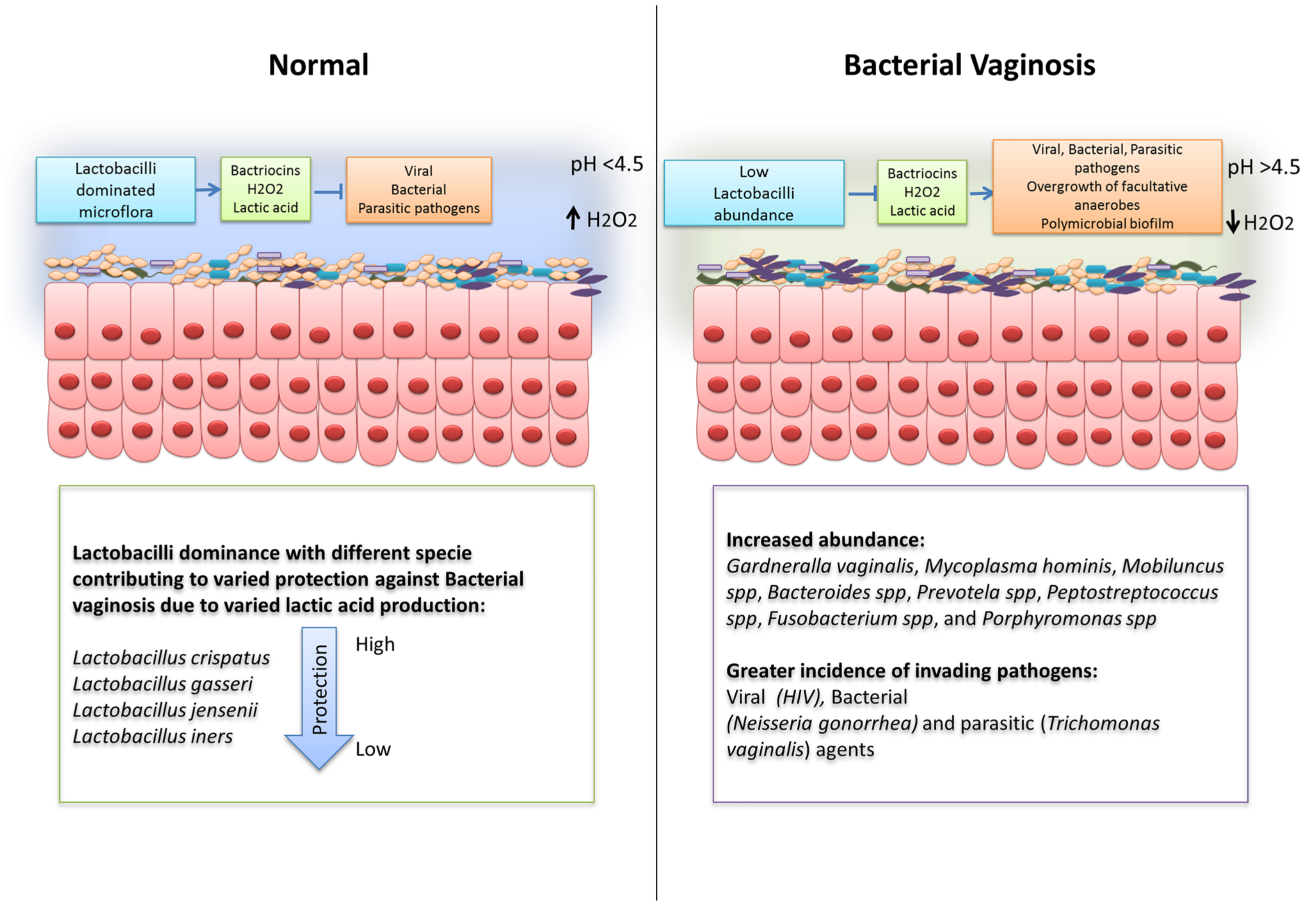

Fig. 1 Normal vaginal flora vs. Bacterial vaginosis. Normal vaginal microflora is marked by lactobacilli dominance with different specie contributing to varied protection against Bacterial vaginosis due to varied lactic acid production with a low abundance of *Gardneralla vaginalis*, *Mycoplasma hominis*, *Mobiluncus* spp., *Bacteroides* spp., *Prevotela* spp., *Peptostreptococcus* spp., *Fusobacterium* spp., and *Porphyromonas* spp. as well as lower incidence of invading pathogens. Typically during bacterial vaginosis, there is lower lactobacilli abundance and increased abundance of *Gardneralla vaginalis*, *Mycoplasma hominis*, *Mobiluncus* spp., *Bacteroides* spp., *Prevotela* spp., *Peptostreptococcus* spp., *Fusobacterium* spp., and *Porphyromonas* spp. and greater incidence of invading pathogens like viral *(HIV)*, bacterial *(Neisseria gonorrhea)* and parasitic (*Trichomonas vaginalis*) agents

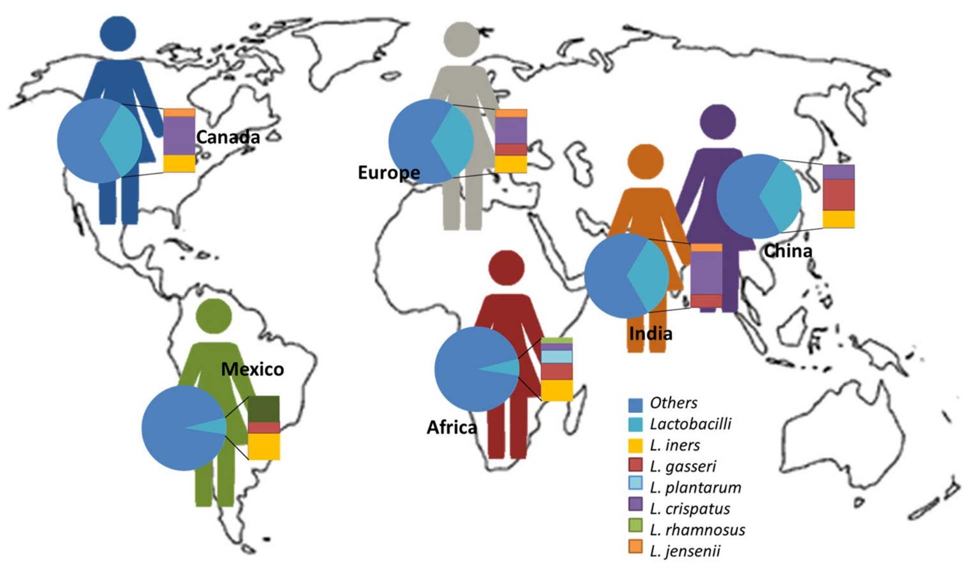

Fig. 2 Variation in lactobacilli abundance and species diversity among normal healthy women of reproductive age across the globe. The bar length represents comparative abundance of each specie

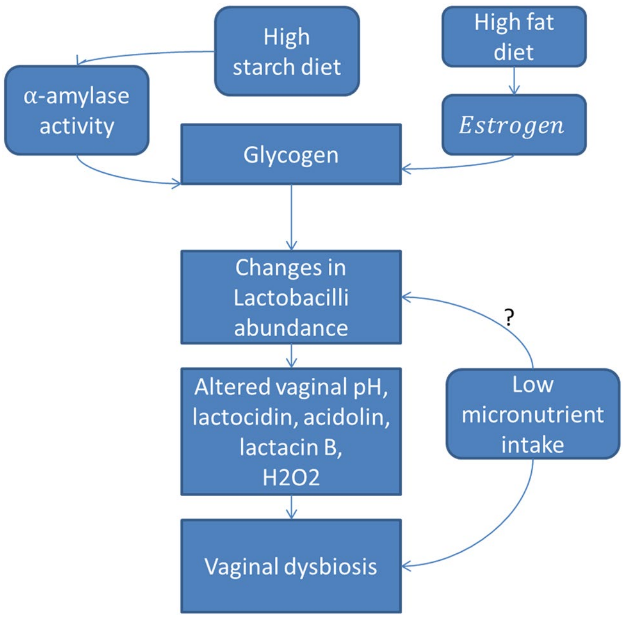

Fig. 3 Proposed mechanism by which changes in diet may influence risk of bacterial vaginosis. Lactobacilli abundance may be influenced by a glycogen-rich environment facilitating growth and lactic acid production. α-amylase activity can in turn affect glycogen availability to *Lactobacillus* strains unable to uptake glycogen directly. Both α-amylase activity and glycogen levels may be regulated by host diet and genetics affecting risk of bacterial vaginosis

vaginal microbiome of healthy women in Canada (Chaban et al. 2014). In contrast, *L. gasseri*, *L. iners*, and *L. crispatus* dominate the vaginal microflora of healthy reproductive-age women in China as determined by denaturing gel electrophoresis (Xiao and Liao 2012). Regional variations in vaginal microbiome are also marked in the Indian population where *L. crispatus*, *L. gasseri*, and *L. jensenii* form the cultivable part of vaginal *Lactobacillus* which was investigated using culture-based approach from vaginal swabs obtained from 47 healthy women (Xiao and Liao 2012).

On the other hand, European women exhibit distinctive vaginal microbiota comprising *L. crispatus*, *L. iners*, *L. gasseri*, and *L. jensenii* (Jespers et al. 2012), whereas a study from Africa reveals the dominance of *L. iners* as a major species in the vaginal microbiota followed by *L. gasseri*, *L. plantarum*, *L. crispatus*, *and L. rhamnosus* (Anukam et al. 2006). The above findings indicate that species-level variations exist in the vaginal flora of healthy women from different regions of the world. These variations may also be attributed to racial differences in the tested populations. For instance, a cross-sectional study comprising 1268 African American subjects and 416 European subjects was conducted to evaluate differences in their vaginal microbiota profiles with the help of 16 s rRNA gene analysis. It revealed that the women of European ancestry had vaginal microbiome profiles dominated by *L. crispatus* as compared to Afro-American women who had *L. iners* dominated vaginal microbiota in the majority of subjects. Additionally, the probability of harboring *Lactobacillus* species dominated microflora was found to be higher among European women as compared to women of African American descent (Fettweis et al. 2014).

Vaginal microbiome profile contrasts among women of different ethnic backgrounds. A descriptive study comprising 144 healthy adult Black and Caucasian women revealed that women of Black origin were less likely to possess vaginal communities dominated by lactobacilli (7%) as compared to Caucasian women (33%). Additionally, vaginal microbial communities comprising a roughly equal number of one or more species of *Lactobacillus* were more prevalent in Caucasian women (Zhou et al. 2007).

Bacterial vaginosis

Bacterial vaginosis is accompanied by a shift in vaginal microbiota with a subsequent loss of protective *Lactobacillus* species and a concomitant increase in the abundance of facultative and anaerobic organisms in the vaginal microenvironment. Clinically, it manifests as foul smelling vaginal discharge, burning sensation during urination, and itching around and outside the vagina. The prevalence of bacterial vaginosis in the United States has been reported to be around 29% while it is 26% in Sweden (Koumans et al. 2007; Moi 1990).

There are multiple risk factors associated with bacterial vaginosis including; vaginal douching, multiple sex partners, smoking, intra-uterine device usage, use of scented soaps, and history of vaginal infection (Holzman C et al. 2001; Smart et al. 2004; Georgijevic et al. 2000). Black women are more vulnerable to bacterial vaginosis as compared to white women. This can be explained by the fact that the composition of vaginal flora of black women is different from that of white women and they harbor a wide array of facultative and anaerobic commensals in their vagina. Furthermore, black women do not have *Lactobacillus* dominant microflora which explains the enhanced vulnerability to overgrowth of pathogenic organisms in vagina (Ness et al. 2003).

Disruption in normal ecological balance leads to the overgrowth of several anaerobes which include *Gardnerella vaginalis*, *Mycoplasma hominis*, *Mobiluncus* spp., *Bacteroides* spp., *Prevotela* spp., *Peptostreptococcus* spp., *Fusobacterium* spp., and *Porphyromonas* spp. The loss of lactobacilli impairs the natural protective mechanism leading to a higher than normal pH (> 4.5) as a result of lactic acid depletion (Georgijevic et al. 2000; Wijgert et al. 2014).

Bacterial vaginosis is usually diagnosed according to two criteria: Amsel criteria and Nugent score criteria. According to the Amsel criteria, three of four findings must be observed, that is, presence of clue cells on wet mount microscopy, fishy odor after the addition of 10% KOH solution in vaginal fluid, vaginal pH > 4.5, and thin homogenous vaginal discharge. Nugent scoring criteria are based on microscopic visualization of three bacterial morphotypes. Nugent score of 0–3 is characterized as normal; 4–6 as intermediate microbiota and 7–10 is the diagnostic criteria of bacterial vaginosis (Sha et al. 2005).

The etiology of bacterial vaginosis is complex involving several factors, however, the underlying abnormality is the characteristic shift in the vaginal flora. Culture-independent molecular approaches have made significant advances towards the understanding of the relative abundance and diversity of vaginal microbiota in diseased state. A number of non-cultivable bacterial pathogens have been identified with molecular techniques and have been categorized as bacterial vaginosis-associated bacteria (BVAB). A cross-sectional study of 50 women suffering from bacterial vaginosis revealed the abundance of bacteria belonging to three different phyla namely, Firmicutes, Fusobacteria, Bacteroidetes, and genus *Acinetobacte*r by employing DNA finger printing technique (DGGE) (Ling et al. 2010).

Bacterial vaginosis is an independent risk factor for a number of conditions like pre-term birth, low birth weight, acquisition of HIV, and increased tendency to acquire chlamydial and gonococcal infections (Hillier et al. 1995; Petrova et al. 2013; Barbone et al. 1990). Bacterial vaginosis may be symptomatic or asymptomatic depending on the degree of dysbiosis, virulence of colonizing pathogen, and its load (Wijgert et al. 2014).

Dynamics of vaginal microbiome in pregnancy

Pregnancy re-shapes the vaginal microbiome with characteristic changes. It acquires more stability and less diversity at the onset of pregnancy with the dominance of one or more *Lactobacillus* species. A longitudinal study of British women who experienced uncomplicated pregnancies unveiled five distinct community state types (CSTs) in vaginal microbiome analyzed with the help of MiSeq sequencing of 16 s rRNA amplicons. CST-1 (*L. crispatus*) was observed in 40% subjects, CST-III (*L. iners*) in 27% subjects, CST-V (*L. jensenii*) in 13%, CST-II (*L. gasseri*) in 9%, and CST-IV (characterized by reduced lactobacilli and increased number of bacterial vaginosis-associated bacterial species) in 8% subjects (MacIntyre et al. 2015).

Similar findings have been reported from the USA where *Lactobacillus* species (CST-I, II, III, and V) dominate vaginal microbiota during the course of pregnancy in White and Asian women whereas, CST-1V is more likely to dominate the flora of women of Black and Hispanic descent (Dominguez-Bello et al. 2010). In the Mexican population, CST differences exist compared to European and American women. *L. acidophilus* was isolated from 78% pregnant Mexican women followed by *L. iners* (54%), *L. gasseri* (20%), and *L. delbrueckii* (6%) (Hernández-Rodríguez et al. 2011).

Different species of *Lactobacillus* have a different impact on the stability of the entire vaginal microbiota. *L. crispatus* is believed to increase the stability of vaginal microflora whereas *L. iners* and *L. jensenii* are less proficient in imparting stability and hence predispose the individual to dysbiosis. This finding is validated by Verstraelen et al. (2009), in which vaginal microbiome of 100 Caucasian women was analyzed and it was concluded that *L. crispatus* dominated vaginal flora has a fivefold decreased risk of vaginal dysbiosis compared to vaginal flora dominated by other *Lactobacillus* species (Verstraelen et al. 2009).

Dysbiosis in vaginal microbiome and pre-term birth

World Health Organization defines pre-term birth as babies born alive before completion of 37 weeks of pregnancy. It is the leading cause of neonatal mortality and morbidity and approximately 15 million pre-term births occur every year around the globe affecting the health of mother and children (Organization WHO 2012).

Abnormal vaginal flora is believed to be a potential risk factor for pre-term birth. Women with *Lactobacillus* abundant vaginal flora in the first trimester of pregnancy have a 75% lower risk of delivering pre-term babies compared to those with abnormal flora characterized by colonization of BVAB. Furthermore, species diversity of Lactobacilli is also a critical factor in determining the outcome of pregnancy. A cohort study comprising 111 pregnant women, of which 98 delivered term and 13 delivered pre-term, postulated that women harboring only one species of *Lactobacillus* during pregnancy were at a greater risk of delivering pre-term compared to those who have more than one species as a part of the vaginal microbiota. It also revealed that *L. iners* was the dominant species associated with pre-term birth in pregnant women (Petricevic et al. 2014).

A study by Romero et al., contradicts the idea of a causal relationship between abnormal vaginal flora and pre-term birth. According to their results, no significant difference was found in relation to bacterial taxa, relative abundance and frequency of CSTs in the vaginal microbiome with relation to gestational age when 18 pre-term delivering and 70 term delivering mothers were compared to investigate differences in the microbiota. Limitations of the study in terms of sample size and analysis of local population can be overcome by wider analysis in terms of study subjects belonging to a different race, ethnicity, and region (Romero et al. 2014b).

Changes in vaginal microbiome during menopause

Menopause is defined as a period of permanent cessation of menstruation in women. Clinically, it is identified after 12 months of amenorrhea. It typically occurs at the median age of 51.4 years (Casper 2009). Menopause is accompanied by significant hormonal changes. Among these, a sharp decline in estrogen level is noteworthy. Reduction in estrogen levels leads to vulvo-vaginal atrophy and alteration in the vaginal microbiome (Brotman et al. 2014).

A comparative study involving pre-menopausal, peri-menopausal, and post-menopausal American women has brought to light the changes in vaginal flora in relation to the event of menopause. Vaginal microbiome of post-menopausal women was primarily inhabited by *Streptococcus* spp and *Prevotella* spp and pre-menopausal women had *Lactobacillus* spp (*L. crispatus*, *L. jensenii*, *L. iners*, and *L. gasseri*) dominated microbiota, whereas in peri-menopausal women, *Atopobium* species dominated (Brotman et al. 2014).

There exists an inverse relation between *Lactobacillus* species and vaginal dryness. A study from the United States highlighted the depleting number of *Lactobacillus* spp. in post-menopausal women experiencing vaginal dryness compared to those without vaginal dryness. *L. iners* and *L. crispatus* are found in those post-menopausal women who had not experienced vaginal dryness. The declining estrogen levels consequently increase vaginal dryness and atrophy which ultimately leads to reduction in the load of *Lactobacillus* spp. in vagina (Hummelen et al. 2011).

Studies investigating the vaginal microbiome in post-menopausal women are limited and have been carried out on a small number of samples. To provide conclusive evidence, large population-based studies from around the globe can play an instrumental role.

Vaginal microbiome and infertility

Generally, *Lactobacillus*-dominated vaginal flora is considered a hallmark of normalcy. Bacterial vaginosis-associated vaginal microbiome is believed to be the cause of infertility in women of reproductive age (Mania-Pramanik et al. 2009). An overview of existing literature reveals the incidence of fertility to be 7.4% in American women belonging to age group 15–44 years (Wright et al. 2008). Moreover, women with idiopathic infertility are more likely to have abnormal vaginal flora (Spandorfer et al. 2001).

In vitro studies suggest the important role of vaginal microbiome during embryo implantation and resultant pregnancy outcome. Colonization of vagina with hydrogen peroxide-producing *L. crispatus* has marked influence in increasing the rate of implantation and live birth while reducing the chances of adverse pregnancy outcome (Sirota et al. 2014).

Systemic review and meta-analysis of studies regarding association of bacterial vaginosis and infertility have shown that 19% of infertile women have bacterial vaginosis, followed by 39% who had intermediate vaginal flora. Furthermore, bacterial vaginosis is more common in infertile women compared to fertile women of the same age group and it is associated with reduced rates of conception. These findings strengthen the fact that *Lactobacillus* species abundance is a hallmark of normal healthy vaginal flora (Oostrum et al. 2013).

Impact of diet

The relationship between the quality of food intake and the health status of an individual is well established (Bahr 2007). Recent studies have also demonstrated a link between diet and the gut microbiome. Western diets negatively alter gut microbiome, which subsequently negatively impacts the health of the host (David et al. 2014). Interestingly, several studies have determined that poor micronutrient intake, especially vitamins A, C, E, and D and β-carotene, folate, calcium increases the risk for bacterial vaginosis (Thoma et al. 2011). Furthermore, an increased risk of bacterial vaginosis occurs in women with high energy and total fat consumption (Thoma et al. 2011; Neggers et al. 2007).

As mentioned in earlier sections, *Lactobacillus* sp. abundance confers a protective vaginal microenvironment to the host. Glycogen is important for lactobacilli growth and is utilized by the bacteria to yield lactic acid as a by-product. Therefore, vaginal pH decreases with increasing glycogen concentrations (Mirmonsef et al. 2014). Low vaginal pH and anti-bacterial compounds secreted by lactobacilli, including lactocidin, acidolin, lactacin B, and hydrogen peroxide (H_2O_2) confer protection against colonization by other virulent microbes (Mirmonsef et al. 2014). It is speculated that high levels of glycogen, as a result of high-starch intake, promote glycogen secretion by the vaginal mucosa and the proliferation of lactobacilli whose abundance is unique in human females compared to other mammals (Miller et al. 2016).

Apart from glycogen, the enzyme α-amylase is also important in breaking down glycogen into a form usable by lactobacilli strains that cannot metabolize glycogen directly

(Spear et al. 2014; Nasioudis et al. 2015). Evidence from studies on human cohorts that consume more starch suggests that agrarian societies as opposed to hunter gatherers possess more copies of salivary amylase genes and, in turn, produce more amylase (Perry et al. 2007). A shift to diets rich in starch transforms vaginal microbial communities as is evident in women with different ancestries. Therefore, Miller and colleagues propose a "diet hypothesis" to explain *Lactobacillus* abundance in human vaginal tract (Miller et al. 2016).

This is supported by studies suggesting a role of diet in vaginal microbial composition, particularly with regard to risk of bacterial vaginosis (Thoma et al. 2011; Neggers et al. 2007; Tohill et al. 2007). However, one study investigating the role of a high-starch diet on vaginal glycogen levels in humans saw no glycogen change in response to high-starch intake (Willson and Goforth 1942). Other studies show that differences in women's diet predict differences in glycogen levels in the vagina. For instance, a BMI greater than 30 has been linked to increased free glycogen in vaginal fluid (Mirmonsef et al. 2014). Variation in vaginal pH and community composition among human populations has been discussed in earlier sections but this variation is typically matched to race rather than to genotype, and it is difficult to dissect genotypic variation with changes in diet.

Hormonal influences in altering vaginal microbiota during pregnancy have been widely reported. Estrogen is primarily responsible for mobilizing free glycogen in the vaginal epithelial cells (Fettweis et al. 2014). High-fat diet may increase estrogen levels, for instance, mice fed with a high-fat diet show elevated levels of serum estradiol (Hilakivi-Clarke et al. 2002). Similarly, women switching from a high-fat to a low-fat and high-fiber diet had significant decreases in serum estrogen levels (Goldin et al. 1994). Vegetarian women have low serum estrogen levels compared to non-vegetarian premenopausal women (Goldin et al. 1982). Therefore, we propose that a high-fat and low-fiber diet as well as high-starch intake is likely to alter vaginal microbiota by influencing lactobacilli abundance either directly by influencing glycogen availability or indirectly by estrogen-mediated modulation of glycogen reserves.

Impact of probiotic therapy on vaginal microbiome

World Health Organization defines probiotics as 'living microorganisms which when administered in adequate amounts confers a health benefit on the host (Hotel and Cordoba 2001). Species belonging to genera *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, *Enterococcus*, and *Escherichia* are used as probiotics (Guarner and Schaafsma 1998). The history of probiotics use dates back to biblical times when fermented products were used as nutritional and therapeutic agents (Żukiewicz-Sobczak et al. 2014).

Recent advances in the development and clinical use of probiotics have opened new avenues in therapeutics. It has greatly helped to overcome the phenomenon of growing resistance among pathogens due to improper use of antibiotics in terms of suitability, dosage, and administration. Probiotic treatment has been successful in treating bacterial vaginosis and restoring the normal microbiome in vagina. Once or twice daily oral administration of encapsulated *L. rhamnosus* GR-1 and *L. fermentum* RC-14 strains transforms bacterial vaginosis-associated microbiota to normal microbiota marked by dominance of *Lactobacillus* (Reid et al. 2001).

Probiotics have also been effective in the treatment of altered vaginal microbiome in vulvo-vaginal candidiasis (VVC). Hillier et al., investigated the changes in vaginal microbiota in 7918 pregnant women suffering from VVC and found that vaginal microbiota could oscillate between normal (dominated by *Lactobacillus*) or abnormal (reduced lactobacilli) in VVC (Hillier et al. 1992). Clinical trials have indicated the effectiveness of *L. acidophilus*, *L. rhamnosus* GR-1 and *L. fermentum* RC-14 in restoring *Lactobacillus*-dominated vaginal flora (Falagas et al. 2006).

Conclusion

The normal vaginal microflora is a constantly changing environment influenced by a wide variety of physiological and environmental factors. Lactobacilli seem to play a central role in maintaining a healthy vaginal microenvironment. Vaginal dysbiosis involves changes in the microbial diversity or abundance especially of *Lactobacillus* sp. or certain anaerobic bacteria which promotes inflammation resulting. Vaginal dysbiosis can be a crucial factor in increasing the hosts' risk for STDs, pre-term birth and infertility.

Research highlighting the efficacy of certain probiotic candidates has come to attention in recent years. We believe that educating young women about vaginal dysbiosis and the practices promoting vaginosis as well as the impact of probiotics by medical practitioners are needed.

Authors' contributions SAS and VSS performed the literature review and compiled the initial draft. Both authors contributed equally. HB and PMG contributed to critical review, editing, and approved the final draft. SJ and AA contributed to writing, editing, and prepared the graphic art.

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