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ROLE OF MICROBIOME IN RECURRENT PREGNANCY LOSS: AN INTEGRATIVE STUDY WITH AYURVEDIC AND MODERN PERSPECTIVES

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ABSTRACT

Recurrent abortion (RA), defined as the loss of two or more consecutive pregnancies before 20 weeks of gestation, remains a major global reproductive concern, with nearly half of the cases having no identifiable cause. Recent studies highlight the pivotal role of the human microbiome—particularly vaginal, endometrial, and gut microbial ecosystems—in pregnancy maintenance. Dysbiosis, characterized by decreased Lactobacillus dominance and overgrowth of pathogenic species such as Gardnerella vaginalis and Mycoplasma hominis, disrupts immune tolerance and cytokine balance, leading to inflammation and recurrent pregnancy loss (RPL). A Lactobacillus-dominant vaginal microbiome maintains acidic pH, prevents pathogenic invasion, and promotes implantation, whereas its imbalance correlates with infertility and abortion.[5,12] Similarly, the gut microbiome influences maternal immunity and hormone regulation, linking microbial health to reproductive success. In Ayurveda, recurrent miscarriage corresponds to Garbhasrava and Garbhapata, primarily caused by Vata vitiation along with Pitta and Rakta dushti. Classical texts describe factors influencing conception

through Garbhasambhava Samagri—Ritu, Kshetra, Ambu, and Beeja—and sustaining pregnancy through Garbhasthapaka dravyas. Disturbance in these elements leads to impaired Garbha poshana and fetal loss. The Ayurvedic notion of Krimi (microorganisms) aligns with the modern concept of microbial dysbiosis. Therapeutically, Ayurveda advocates Ahar, Vihar, Rasayana chikitsa, and Garbhas thapana measures. A pilot study using the Ayurvedic formulation TAB-GM, containing Rasayana and Garbhasthapana herbs, showed successful pregnancy continuation beyond 20 weeks in all participants. Integrating microbial modulation (probiotics, diet) with Ayurvedic approaches may restore Dosha-samyata and Kshetra-shuddhi, offering a holistic framework for managing recurrent abortion.

KEYWORDS: Recurrent abortion, microbiome, vaginal dysbiosis, Garbhapata, Ayurveda, Lactobacillus, Garbhasthapak dravayas.

INTRODUCTION

Recurrent abortion (RA), also referred to as recurrent pregnancy loss (RPL), is a distressing reproductive condition that affects approximately 1–2% of women of reproductive age.[1] It is clinically defined as the loss of two or more consecutive pregnancies before 20 weeks of gestation. The etiology of RPL is multifactorial, encompassing genetic, anatomical, hormonal, immunological, and infectious factors. However, in nearly half of the cases, no specific cause can be identified, classifying them as idiopathic. In recent years, growing evidence has highlighted the significant role of the human microbiome in reproductive health, providing new perspectives on the pathophysiology of unexplained pregnancy losses.[3]

The human microbiome represents a complex community of microorganisms inhabiting various regions of the body, including the gut, vagina, and endometrium. Among these, the vaginal microbiome—dominated by Lactobacillus species—plays a crucial role in maintaining an acidic environment, producing antimicrobial compounds, and preventing colonization by pathogenic organisms. Disruption of this delicate balance, termed vaginal dysbiosis, leads to a reduction in Lactobacillus dominance and an overgrowth of anaerobic bacteria such as Gardnerella vaginalis and Mycoplasma hominis.[5] This microbial imbalance can alter local immune responses, induce inflammation, and hinder embryo implantation, ultimately contributing to bacterial vaginosis (BV), infertility, preterm birth, and recurrent miscarriage. Furthermore, recent research suggests that gut microbial dysbiosis influences hormonal metabolism, systemic inflammation, and immune modulation—linking gut health to reproductive outcomes and recurrent abortion.[8]

From the Ayurvedic standpoint, recurrent miscarriage finds its parallel in the conditions termed Garbhasrava (early pregnancy loss) and Garbhapata (late pregnancy loss). Classical texts such as Charaka Samhita, Sushruta Samhita, and Kashyapa Samhita describe the essential factors for conception and fetal sustenance under the concept of Garbhasambhava Samagri, which includes Ritu (fertile period), Kshetra (healthy uterus), Ambu (nutritional essence), and Beeja (ovum and sperm). Imbalance or vitiation in any of these factors, particularly due to Vata aggravation along with Pitta and Rakta dushti, can impair Garbha poshana (fetal nourishment), resulting in miscarriage. Conditions like Yoni vyapad, Jataharini, and Bandhyatva are also described as causative or contributory factors.[26,29]

Ayurveda emphasizes preventive and curative measures through Ahar (wholesome diet), Vihar (healthy lifestyle), Rasayana Chikitsa (rejuvenation therapy), and Garbhasthapana dravyas (pregnancy-sustaining herbs) to ensure Dosha-samyata (homeostasis) and Kshetra shuddhi (uterine purification). Interestingly, these Ayurvedic principles align with modern findings regarding the role of the microbiome in maintaining internal equilibrium and reproductive wellness. Hence, integrating Ayurvedic concepts with microbiome-based research offers a promising, holistic, and individualized approach to understanding and managing recurrent abortions.[46]

Study Design

A narrative review was conducted using PubMed, Scopus, and Google Scholar databases. Keywords included: “microbiome and recurrent pregnancy loss,” “vaginal microbiota and miscarriage,” “endometrial dysbiosis,” and “gut microbiome and reproduction.”.[5] Articles published between 2015 and 2024 were reviewed. Both clinical and experimental studies investigating microbiome composition and recurrent abortion were included. Data on mechanisms, immune regulation, and therapeutic approaches were extracted.[8]

AIM AND OBJECTIVE

PrimaryAim

To Evaluate the Role of Microbiome in Recurrent Pregnancy Loss and correlating its mechanisms and therapeutic possibilities with Ayurvedic concepts of Garbhasrava and Garbhapata.

OBJECTIVES

- To Analyze the Ayurvedic understanding of Recurrent Miscarriage in terms of Garbhasrava, Garbhapata and Garbhasambhava Samagri.
- To Highlight Future Research Directions for Clinical Evaluation of Microbiome insights for Prevention and Management of Recurrent Abortion.

MATERIAL AND METHOD

All classical Ayurvedic texts including Brihatrayee, Laghutrayee, and other relevant literature on Garbhasrava were reviewed. Articles related to microbiome and recurrent pregnancy loss were also considered to correlate Ayurvedic concepts with modern evidence.

Conceptual Study

Conception is not just a biological event; it is a sacred, well-orchestrated process influenced by age, health, nutrition, mental state, and environmental purity. Ayurveda describes Garbhotpatti (conception) holistically, ensuring a healthy pregnancy and the birth of a child. The essential aspects of reproduction can be grouped into the following key elements:

1. Understanding the Ideal Age for Conception (Garbhadhana Yogya Aayu)

- **Charaka Samhita:** Recommends 16 years as suitable age for conception due to Samatvagatveerya (excellent reproductive vitality), indicating Mugdha (up to 19 years) as developmental phase.[30]
- **Modern Evidence:** Pelvic ossification concludes around 20–21 years, confirming physical reproductive readiness occurs after 16 years.[27]

2. The Four Pillars of Conception (Garbha Sambhava Samagri).[33]

Factor	Role in Conception	Probable Adverse Outcomes (Imbalance)
Ritu	Fertile period during which ovulation occurs.	Infertility, failure of conception
Kshetra	Healthy uterus provides suitable environment for fertilization and early fetal development.	Ectopic pregnancy, miscarriage, infertility
Ambu	Nourishment from maternal fluids(Rasa) supports fetal growth.	Premature birth, low birth weight, developmental issues
Beeja	Male and female gametes; foundation of embryo.	Infertility, congenital defects, hereditary issues

3. Garbhadhana Vidhi (Preconception Care)

A. Detoxification & Cleansing (Shodhana Karma)

Both partners should undergo cleansing therapies (e.g., Vamana, Virechana, Anuvasana, Asthapana Basti) to eliminate risk factors.[28]

B. Psychological & Emotional Preparation

- Putreshti Yajya (For Healthy Progeny)and other rituals promote mental stability, happiness, and environmental purification.[45]

C. Signs of Ovulation (Ritumati Lakshanas)

- Physical changes such as facial glow, flanks and eye laxity, increased libido.
- Timing coitus on even or odd days may influence gender of the child, reflecting ancient understanding of reproductive physiology.

4. Process of Descent of Various Components within Embryo (Garbhavakranti)

- Embryo is composed of **Shadbhutas (six elements)**: spiritual (Satva & Atma) and physical (Panchamahabhuta).
- Nutrient transport occurs through **Upsneha (Snigdhatva)** and **Upsweda (Utkleda)**, ensuring fetal development.

5. Garbhasrava

A. Definition and Classical References

- Garbhasrava refers to miscarriage before complete formation of placenta and amniotic membranes (up to 4 months).
- Acharya Bhoja: 1st three months; Bhel Samhita: up to two months.
- Related concepts: Yonivyapada, Jataharini, Bandhya.

B. Aetiological Factors of Garbhasrava and Garbhapata

- Harmful food habits and lifestyle (Garbhaupghatakara Bhavas) may lead to abortion, intrauterine death, or fetal demise.
- Classical texts detail specific dietary, lifestyle, and environmental factors.
- From third Paksha (45 days) to fifth month, unfulfilled fetal desires (Douhrida) may result in Garbhavinasha.[46]

C. Samanya & Vishistha Nidana

- Charaka, Sushruta, Harita, Bhel, and Kashyapa texts outline causes ranging from vitiated doshas, physical trauma, infections, chromosomal abnormalities, to psychological and environmental factors.

D. Symptoms (Lakshana) of Garbhasrava

- **Samanya:** Vaginal bleeding (Pushpam Pashyet), uterine pain (Garbhashaya Shula), sacral and groin pain.
- **Vishistha:** Yonivyapada types, Raktyoni, habitual abortion patterns.

E. Management of Recurrent Abortion

1. Before Conception

- Strengthen reproductive health through Rajaswalacharya, Garbhadhana Vidhi, and treatment of Yonivyapada, Jataharini, Bandhya.[45]

2. After Conception

- **Before Abortion:** Nidanaparivarjanam, Ama Garbha Chikitsa, Sthanantara Gamita Garbha, Recurrent Bleeding treatment, Masanumasika Chikitsa, treatment of Pariharya Garbha.
- **After Abortion:** Laghupanchmula Siddha Peya, Tila-Uddalaka Yavagu.

MODERN ASPECT OF ROLE OF MICROBIOME IN RECURRENT ABORTION

1. Vaginal Microbiome

Healthy pregnancies are generally linked with Lactobacillus-dominant vaginal flora that produce lactic acid, maintaining an acidic pH that protects against pathogens. Women with recurrent abortion often show higher microbial diversity and pathogenic colonization, including Gardnerella vaginalis, Atopobium vaginae, Prevotella species, and Ureaplasma urealyticum. Vaginal dysbiosis promotes inflammation and increases the risk of ascending infections, contributing to miscarriage.

Cervicovaginal microbiome analysis in RPL patients revealed the following patterns

- **Increased taxa:** Delftia, Microbacterium, Anaerobacillus, Cutibacterium, Chloroplast, Streptococcus.
- **Reduced taxa:** Lactobacillus, Bifidobacterium.

2. Endometrial Microbiome

The endometrium hosts a low-biomass microbiome essential for uterine receptivity. In RA patients, Lactobacillus is often reduced, while colonization by Streptococcus, Staphylococcus, and Escherichia coli increases. Dysbiotic endometrium alters cytokine profiles, elevating IL-6 and TNF-α, and impairs implantation.[12]

Chronic endometritis in RPL cases often shows elevated Enterococcus, Streptococcus, Atopobium, and Gardnerella vaginalis. Reduced Lactobacillus crispatus along with the presence of Gardnerella vaginalis and fungi is strongly associated with RPL. Lactobacillus iners, a less protective species, is frequently observed in women experiencing miscarriage. Studies indicate that L. crispatus dominance supports healthy term pregnancies, while L. iners dominance correlates with pregnancy loss.[11]

3. Gut Microbiome and Systemic Effects

The gut microbiome plays a key role in systemic immunity and hormone metabolism. RA patients demonstrate reduced short-chain fatty acid-producing bacteria, which contributes to inflammation and impairs the Treg/Th17 balance. Such dysbiosis may indirectly increase the risk of pregnancy loss through immune and metabolic disturbances.

4. Mechanistic Insights

- **Immune dysregulation:** Microbiome imbalance shifts maternal immune tolerance toward a pro-inflammatory state.
- **Chronic endometritis:** Dysbiosis increases subclinical infections, impairing implantation.
- **Metabolic effects:** Gut microbiota imbalance alters estrogen metabolism and immune homeostasis.

Immune-Metabolite Interactions

- Vaginal leukocytes correlate with IL-6 and IL-8; high IL-8 predicts Candida infection.
- Candida infection correlates with O-acetylcholine, glucose, choline, and 4-hydroxyphenyllactate.
- Glycine, serine, and lactate inversely correlate with cytokine levels.

Metabolic Shifts: Dysbiosis increases acetate, propionate, and biogenic amines (cadaverine, putrescine) while decreasing protective metabolites like lactate, glycine, and leucine.

Barrier Dysfunction: Biofilm formation and altered epithelial homeostasis facilitate co-infections, increasing miscarriage risk.

Pathophysiological Mechanisms

- Overactivation of pro-inflammatory cytokines and suppression of regulatory T cells.
- Epithelial barrier disruption by biofilms and pathogen invasion.
- Systemic inflammation mediated by gut microbiota-driven Th1/Th17 responses affecting maternal-fetal tolerance.

Commensal species such as Lactobacillus crispatus exhibit immunomodulatory effects, countering inflammation and enhancing maternal-fetal tolerance. Vaginal transplantation of L. crispatus has been shown to improve immune tolerance and pregnancy outcomes.

5. Limitations in Vaginal Microbiome Studies

Despite technological advancements, challenges remain:

- Variability in sequencing and analysis complicates standardization.
- Vaginal dysbiosis increases early pregnancy loss risk but may not significantly affect live birth rates.
- Limited evidence links first-trimester fetal loss with preterm birth in IVF.
- BV-associated pregnancy loss varies regionally, requiring research into environmental and socio-economic factors.
- Treatment protocols may alter the vaginal microbiome, potentially influencing RPL outcomes.

6. Therapeutic and Future Perspectives

1. **Microbiota Transplantation:** Vaginal microbiota transplantation from screened donors may restore microbial balance and support live births in RPL.
2. **Probiotics/Prebiotics:** Supplementation with Lactobacillus, especially L. crispatus, may restore protective flora.
3. **Targeted Antimicrobials:** Eliminate pathogenic overgrowth while preserving commensals.
4. **Personalized Medicine:** Microbiome profiling could help predict and prevent miscarriage.

7. Observational Clinical Study

Patient Profile: Nine women aged 20–35 years with a history of spontaneous abortion received Tab GM 1 BD for four months, with monthly follow-up up to 20 weeks of pregnancy.

Most participants displayed moderate activity, good bowel and urinary function, and normal systemic parameters. Low Vyayama and Jarana Shakti along with Vishama/Manda Agni suggest reduced metabolism, possible nutritional deficiencies, and compromised reproductive strength. Raja-dominant Manasa Prakriti may indicate emotional stress, affecting hormonal balance and pregnancy maintenance.

Treatment History

DISCUSSION

The microbiome is integral to reproductive health, and accumulating evidence indicates its role in recurrent abortion. Dysbiosis of the vaginal and endometrial microbiota can impair implantation, while alterations in the gut microbiome may disrupt systemic immunity and hormonal balance, increasing vulnerability to pregnancy loss.

Clinical Implications

- **Diagnostics:** Profiling of the microbiome may serve as a biomarker for unexplained recurrent abortion.
- **Therapeutics:** Interventions including probiotics, prebiotics, and selective antimicrobial therapies can help restore microbial equilibrium.
- **Preventive Strategies:** Dietary approaches that support short-chain fatty acid-producing gut bacteria may improve immune tolerance and reproductive outcomes.

Limitations

Existing studies are mostly small, observational, and methodologically varied. Well-designed longitudinal trials are needed to establish causality and elucidate the mechanistic links between microbiome alterations and recurrent abortion.

Ayurvedic Perspective

Ayurveda provides a holistic framework for understanding recurrent abortion, encompassing physical, psychological, and environmental influences. Key principles include:

- **Garbhadhana Yogya Ayu:** Maternal age plays a critical role, with preterm birth and abortion linked to very young (Atibala) or advanced (Ativriddha) maternal age.
- **Garbhadhana Vidhi (Preconception Care):** Emphasizes reproductive optimization through detoxification, balanced diet, and lifestyle interventions that promote healthy fetal development.
- **Garbha Sambhav Samagri:** The four essential elements—Ritu (fertile season), Kshetra (uterus health), Ambu (adequate nutrition), and Beeja (quality gametes)—are crucial for conception and fetal growth.

Ayurvedic texts also highlight harmful influences on pregnancy, such as unsuitable diet, lifestyle choices, and mental stress, collectively referred to as **Garbhaupghatakar Bhavas**. Specific conditions provide insight into the etiology of abortion:

- **Putraghni and Asrja Yonivyapda:** Indicate infective causes of pregnancy loss.
- **Jataharini:** Suggests environmental or psychological factors.
- **Garbhasravi Bandhya and Adibandhya:** Correlate with recurrent abortions of unknown origin.
- **Raktbandhya:** Points to immunological causes.
- **Vatabandhya:** Associated with chromosomal or genetic abnormalities.

While Ayurvedic interventions show potential, rigorous scientific validation is necessary to integrate traditional knowledge with modern clinical practice, enabling a comprehensive and holistic approach to managing recurrent abortion.

Future Directions

Future research should focus on combining microbiome profiling with immunogenetic studies, developing personalized microbial therapies, and conducting clinical trials to evaluate probiotics and targeted interventions in recurrent abortion management.

CONCLUSION

The human microbiome is a pivotal yet underexplored determinant in recurrent abortion. Dysbiosis across the vaginal, endometrial, and gut microbiota can impair immune tolerance and elevate inflammatory responses, thereby increasing the risk of pregnancy loss. Microbiome-focused diagnostics and targeted interventions offer potential for improving outcomes in unexplained recurrent abortion.

Nonetheless, the link between vaginal microbiome imbalance and recurrent pregnancy loss warrants further validation through large-scale, well-controlled clinical trials. Individual variations in microbiome composition throughout pregnancy pose challenges in identifying uniform metabolite shifts and immune responses. Establishing standardized biomarkers, such as specific Lactobacillus taxa, along with pre-screening participants for environmental and genetic factors, will strengthen study reliability.

Ayurveda provides a holistic framework for understanding and managing recurrent abortion by addressing underlying doshic imbalances, promoting detoxification, and supporting psychological well-being. Integrating these traditional strategies with modern medical approaches may enhance maternal and fetal health outcomes.

These results underscore the potential of Ayurvedic interventions as complementary approaches within a multidisciplinary management strategy for recurrent pregnancy loss, particularly when conventional therapies are limited or ineffective. Future large-scale studies with longer follow-up periods are necessary to confirm these findings and elucidate the mechanisms of action of the herbal constituents, contributing to the scientific validation and clinical integration of Ayurvedic therapeutics in modern reproductive healthcare.

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