

## EXPLORING THE AGNI–GUT MICROBIOTA AXIS IN FEMALE INFERTILITY: AN INTEGRATIVE REVIEW

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### ABSTRACT

**Aim:** To explore the role of *Agni* and gut microbiota in female reproductive health and infertility through an integrated Ayurvedic and modern scientific perspective. **Background:** Infertility is not merely a medical condition; it can affect the emotional, psychological, social, and marital well being of a couple. Approximately 8%–10% of couples worldwide are affected by infertility. *Agni* plays a central role in digestion, metabolism, and tissue formation, while modern science identifies gut microbiota as a key regulator of hormonal and metabolic balance. This review integrates both perspectives to highlight their relevance in female reproductive health. **Material and Methods:** A narrative conceptual review was conducted by synthesizing classical Ayurvedic texts with peer-reviewed biomedical literature indexed in PubMed, Scopus, and google scholar. Search conducted using Keywords *Agni*, *Aam*, gut microbiota etc. Sources were critically analyzed to identify convergences between Ayurvedic theory and modern science. **Conclusion:** *Agni* maintains the formation and nourishment of *Aartava* and *Shukra Dhatu* via proper *Paka and Rasa Dhatu* formation. Impaired *Agni* leads to *Aamvisha* formation causing *Srotorodha* and *Dosha* vitiation which is responsible for *Bandhyatva*. Modern research shows that gut microbiota regulates estrogen metabolism, insulin sensitivity and the hypothalamic–pituitary–ovarian (HPO) axis. Gut dysbiosis is associated with hormonal imbalances and menstrual irregularities. Thus, the present study highlights Ayurvedic concepts of *Agni* and *Aam* closely correlate with gut microbiota and metabolic dysfunction which directly affects reproductive health. **Clinical Significance:** Restoration of *Agni* through *Pathya Aahara-Vihara* and *Aushadhi* improves hormonal regulation, ovulation, and reproductive outcomes. Thus resulting in good progeny and reducing infertility.

**KEYWORDS:** *Aam*, *Agni*, Conceptual study, Gut Dysbiosis, Gut Microbiota, Infertility.

### BACKGROUND

Infertility is defined as the inability to conceive within one or more years of regular unprotected coitus.<sup>[1]</sup> Acharya Charak has included *Garbha Sambhava Samgri* as an important factor for conception, which are *Ritu* (season or fertile period), *kshetra* (healthy *Yoni*, uterus and passage), *Ambu* (proper nutrient fluid), and *Bija* (*Shukra* and *Sonita*). Abnormality in any one of these can cause infertility.<sup>[2]</sup> Infertility affects a significant proportion of reproductive-aged couples worldwide. 60–80 million couples suffering from infertility every year worldwide, probably between 15 and 20 million (25%) are in India alone. According to a report by the World Health Organization (WHO), one in every four couples in developing countries is affected by infertility.<sup>[3]</sup>

Recent researches have highlighted the significant role of the gut microbiota in regulating metabolic, endocrine, immune, and inflammatory pathways that are essential for normal reproductive function. Alterations in gut microbial composition have been associated with hormonal imbalance, impaired ovulation, and reduced fertility outcomes.

In Ayurveda, *Agni* is the fundamental principle for regulating digestion, metabolism, nutrient assimilation, and nourishment. Proper functioning of *Agni* is considered essential for maintaining health and ensuring the normal formation and functioning of reproductive tissues. Impairment of *Agni* may lead to *Agnimandya* and may cause *Artavavaha Srotodushti*, thereby contributing

to infertility. Thus in Ayurveda, *Agni* is considered the fundamental determinant of health and metabolism.

*Agni* and gut microbiomes, both are recognized for metabolic homeostasis. However, the relationship between *Agni*, gut microbiota, and infertility remains inadequately explored. Therefore, the present study was undertaken to evaluate the potential role of *Agni* and gut microbiota in female infertility and to explore the conceptual parallels between Ayurvedic and contemporary science. The literature retrieved from Ayurvedic Samhitas and peer-reviewed articles from different databases has been summarized below.

### Importance of Garbha Sambhava Samgri

According to Acharya Charak, abnormalities of *Ritukala*, *Yoni*, *Ambu*, and *Shukra*, *Aartava* have been included in the causes of delay in achieving conception.

*Akala* yoga or coitus at improper time refers to period of age and *Ritukala* both. In young or old ladies due to pre-menarche and menopausal stage respectively and before or after *Ritukala* due to absence of ovum respectively conception does not take place.

The word *Yoni* refers to entire reproductive system, thus, congenital or acquired diseases of anatomic components of reproductive organs can be included. Normal or healthy state of *Kshetra* (uterus or passage) also indicates importance of healthy condition of reproductive system. Abnormalities of reproductive organs includes gynecologic disorders like *Yonyarsha*, *Yonivyapad*, injury to *Aartavavaha Srotas*, *Garbhakoshabhanga*, *Bhaga Sankoch* etc., if not treated properly cause infertility.

*Ambu* or nutrient/dietetic abnormalities causes improper nourishment or *Dhatukshaya* which influences normal secretion of hormones resulting into failure to achieve pregnancy. *Aahara* or dietetic abnormalities cause infertility in three ways i.e. (i) by producing loss of *Dhatu*s, thus, influencing hormones and (ii) by hampering nourishment of fertilized egg or implantation of zygote (iii) by vitiating *Doshas* which cause various gynaecologic diseases, thus infertility.

Abnormalities of sperms along with spermatid fluid cause infertility. *Shukra* also refers to secretions of endocrine glands as well as prostaglandins, abnormalities of these factors also cause infertility. *Shonita* refers to ovum, menstrual blood and ovarian hormones. Abnormalities in ovum, ovulation and ovarian hormones produce infertility. *Aartava* vitiated by different *Doshas* produces infertility due to destruction of its *Bija*.<sup>[4]</sup>

### Role of Agni and Aam in Vyadhi Utpatti

Acharya Charak has explained the importance of *Agni* by considering that *Dehagni* is the cause of life, complexion, strength, health, nourishment, lustre, *Oja*, *Teja* and *Prana* (life). *Agni* is responsible for *Pratham Rasa Dhatu* formation from *Aahara Rasa* through proper

*Paka* of *Aahara*. *Agni* has been divided into 13 types, i.e. one *Jatharagni*, five *Bhutagni* and seven *Dhatvagni*. *Jatharagni* is the most important one, which digests food firstly and transforms it into *Prasad Bhaga* (essence) and *Kitta Bhaga* (excrete). *Prasad Bhaga* is responsible for the nourishment of *Dhatu*s and *kitta* is excreted out of the body.<sup>[5]</sup> After that the five *Bhutagni* act on the respective *Bhutika* portion of the *Aahara* and thereby nourishing that particular *Bhutas* in the body. Then seven *Dhatvagni* act on the respective *Dhatu* by which each *Dhatu* is nourished. Thus, *Agni* can be defined as the physiological capacity of the body to digest and metabolize food.

If *Jatharagni* becomes weak (*Agnimandya*) due to *Apathya Aahara Vihara* then improper *Paka* of *Aahara* leads to *Aamvisha* formation in body which leads to Vitiating of *Dosha*. *Aamvisha* blocks *Rasavaha Srotas* and *Aartavavaha Srotas*. As a result, *Vikruta Rasa Dhatu* is formed which in turn affects *Aartava* as *Aartava* is *Updhatu* of *Rasa Dhatu*. The vitiated *Doshas* stagnates where "*Kha Vaigunya*" is available in the body which ultimately manifests as various gynecological disorders such as PCOS, menstrual irregularities and infertility. Hence, *Agni* holds a pivotal role in the proper formation, nourishment, and regulation of *Aartava Dhatu*, which is essential for maintaining female reproductive health. A balanced *Agni* ensures optimal digestion and metabolism, leading to the production of high-quality bodily tissues and the smooth functioning of physiological processes. According to modern science gut microbiota functions same as *Agni*.<sup>[6]</sup>

### Role of Agni in causing Anartava or Alpartarva

*Kapha Vardhaka Ahara* and *Vihara*, results in *Mandagni*. This *Mandagni* results in the formation of *Aam*. *Kapha* along with the *Aam* first vitiates the *Rasa Dhatu*. As *Aartava* is the *Upadhatu* of *Rasa Dhatu*, the *Aartava* gets vitiated. The vitiated *Kapha* along with the *Aam* obstructs the *Aartava* in the *Aartavavaha Srotas* thereby leading to *Anartava* (Amenorrhea) or *Alpartarva* (oligomenorrhea).<sup>[7]</sup>

### Gut microbiota's normal functioning

The gut microbiota or gut flora refers to the complex community of microorganisms, including bacteria, viruses, fungi, and other microbes, that live in the digestive tracts of humans. This inhibits and maintains the homeostasis of gastrointestinal tract and also communicates with other organ systems of body to function normally through the axis, which is referred to as the gut axis. The gut microbiota has broad impacts, including effects on colonization, resistance to pathogens, maintaining the intestinal epithelium, metabolizing dietary and pharmaceutical compounds, controlling immune function, and even behaviour through the gut-brain axis. Imbalances in the gut microbiota (dysbiosis) have been associated with numerous diseases, impaired estrogen metabolism,

disrupt HPO axis, PCOS, insulin metabolism, including certain cancers, and even neurological disorders.<sup>[8]</sup>

### Gut-brain axis

The gut microbiota is a crucial component of the gut-brain axis, a bidirectional communication network between the gastrointestinal tract and the central nervous system. It functions primarily through microbial metabolites such as short-chain fatty acids (SCFAs), neurotransmitters, and modulation of the hypothalamic-pituitary-adrenal (HPA) axis. Alterations in gut microbial composition can disrupt neuroendocrine signaling and hormonal balance, contributing to disorders such as PCOS, anovulation, and infertility.<sup>[9]</sup>

### Gut microbiota relation with reproductive endocrine system

During women's lifetime, gut microbiota plays roles in the reproductive endocrine system influencing hormones such as estrogen, androgen, insulin and other hormones. Gut microbiota trigger estrobolome to produce  $\beta$ -glucuronidase that deconjugates estrogens into their active forms. An imbalance in the microbiome affects microbial diversity, decreases estrogen deconjugation and reduces the circulating active estrogen. Hypoestrogenic state leads to many diseases like PCOS and diabetes. Dysbiosis may even leads to elevated  $\beta$ -glucuronidase activity that may contribute to the development of estrogen-driven diseases like endometrial hyperplasia, fibroids etc all these diseases may be correlated to *Kshetra Dushti* (uterine disease or ovarian diseases).<sup>[10]</sup>

### Gut microbiota relation with ovarian aging changes

Ovarian aging refers to the gradual decline in ovarian function with age. It is characterized by the gradual deterioration in oocyte quantity and quality, accompanied by menstrual cycle irregularity, infertility and finally, the cessation of menses. Estradiol (E2) levels only decrease relatively late during the process of perimenopausal transition. However, plasma E2 levels decreases during the final menstrual cycle, and afterward, the postmenopausal ovaries stop synthesizing E2.<sup>[11]</sup>

### Gut Microbiota and POI

Rather than natural ovarian aging, some women in the population experience a premature decline in ovarian function, that is, premature ovarian insufficiency (POI). POI is a clinical syndrome defined by exhaustion of normal ovarian activity in patients younger than 40 years, which presents as a menstrual disorder (amenorrhea or oligomenorrhea) with elevated gonadotropin levels and low E2 levels. However, it has been noticed that there was a reduction in beta diversity of gut microbiota in patients with POI, which means reduced gut microbial diversity affects reproductive functioning or outcomes. According to Ayurveda, it can be correlated to *Ksheena Artavadushti*, *Artavakshaya* and *Alpaartava*.

### Role of Gut Microbiota in Estrogen metabolism

The human gut microbiota regulates estrogen metabolism through the "estrobolome," the collection of bacterial genes that encode enzymes like  $\beta$ -glucuronidases and  $\beta$ -glucosidases. These enzymes deconjugate and reactivate estrogen, influencing circulating levels. The estrobolome mediates the enterohepatic circulation and bioavailability of estrogen. Alterations in gut microbial composition and estrobolome function have been associated with estrogen-related diseases like breast cancer, endometrial cancer, and polycystic ovarian syndrome (PCOS). This is likely due to dysregulated estrogen signaling partly contributed by the microbial impacts on estrogen metabolism.<sup>[12]</sup>

### Gut Microbiota and HPA axis

The gut-brain axis plays a crucial role in various diseases, where the brain affects gut and gut affects the brain through the vagus nerve. When the brain is stressed the vagus nerve stimulates hypothalamic-pituitary-adrenal axis (HPA axis) to release the cortisol releasing hormone (CRH). This will act on the immunocytes which releases the peptide from the mast cell & other cells, this will cause the destruction in the gut lining that is dysbiosis (*Agnimandya*). Dysbiosis causes the release of metabolites such as the lipopolysaccharides (LPS). Due to the thinning of the gut lining LPS released into the blood stream causing several diseases.<sup>[13]</sup>

### Importance of Samagni

A state of *Samagni* (balanced digestive-fire), representing the normal state of digestive and metabolic factors in Ayurveda, is characterized by optimal and balanced digestion, ensuring efficient nutrient absorption and proper waste elimination. From a microbiota perspective, this state is associated with high microbial diversity, reflecting a resilient and healthy gut ecosystem which means beneficial microbes are abundant. In contrast, *Mandagni* corresponds to reduced microbial diversity, diminished short-chain fatty acid synthesis, gut-brain axis signaling, and heightened disease susceptibility.<sup>[14]</sup>

### MATERIAL AND METHODS

A narrative conceptual review was conducted to examine the potential relationship between the Ayurvedic concepts of *Agni* and *Aam*, the gut microbiota, and female infertility. Classical Ayurvedic texts, including the Charaka Samhita, Ashtang Hridaya, and PV Tiwari were systematically analyzed to identify descriptions of digestive fire, toxin formation, and reproductive health. To complement the traditional perspective, a comprehensive search of peer-reviewed biomedical literature was performed using electronic databases such as PubMed, Scopus, and Google Scholar. The search strategy employed combinations of keywords including *Agni*, *Aam*, gut microbiota, gut dysbiosis, female infertility, reproductive health, hormonal regulation, and metabolism.

**Review Result:** The collected literature was critically appraised to identify conceptual parallels and mechanistic convergences between Ayurvedic theory and contemporary microbiome science. Particular emphasis was placed on understanding how disturbances in *Agni* and the accumulation of *Aam* may correspond to gut microbial imbalance, metabolic dysfunction, and hormonal dysregulation. The synthesis of evidence highlighted that both Ayurveda and modern science converge on the principle that digestive and metabolic integrity is central to reproductive health. In Ayurveda, *Mandagni* leads to *Aam* formation, *Sroto-avrodha* (channel obstruction), and *Dhatukshaya* (tissue depletion), culminating infertility. In modern science, gut dysbiosis disrupts estrogen metabolism, insulin sensitivity, and immune balance, impairing ovulation, implantation, and pregnancy outcomes.

This integrative framework underscores the relevance of Ayurvedic principles in understanding the *Agni*, gut microbiome fertility connection, offering a holistic model that bridges traditional knowledge with contemporary biomedical insights.

## DISCUSSION

Recent biomedical research underscores the pivotal role of the gut microbiota in regulating estrogen metabolism

through the estrobolome, that means a collection of microbial genes capable of metabolizing estrogens. These microorganisms function almost as an extra-organ system, actively participating in maintaining homeostasis and influencing endocrine, immune, and metabolic pathways. Sex hormones such as progesterone, estradiol, and testosterone mediate bidirectional communication between host and microbes, thereby shaping reproductive physiology and neuroendocrine function.<sup>[15]</sup>

Emerging evidence indicates that the human microbiome modulates every stage of female reproduction from folliculogenesis and oocyte maturation to fertilization, implantation, pregnancy, and parturition. Dysbiosis, particularly within the gut ecosystem, disrupts hormonal signaling and immune balance, leading to chronic inflammation and endocrine dysregulation, a phenomenon that closely parallels the Ayurvedic concept of *Aam* formation. Charaka describes *Agni* as the central force of digestion, perception, and nourishment, while *Ashtanga Hridaya* emphasizes that “*Rogah Sarve Api Mandoagne*” that is all diseases arise from impaired *Agni*.<sup>[16]</sup> Sedentary lifestyles and improper dietary habits such as *Adhyasana* (eating before previous food is digested), *Atyasana* (overeating), and *Viruddhasana* (incompatible food combinations) leads to *Agnimandya*.

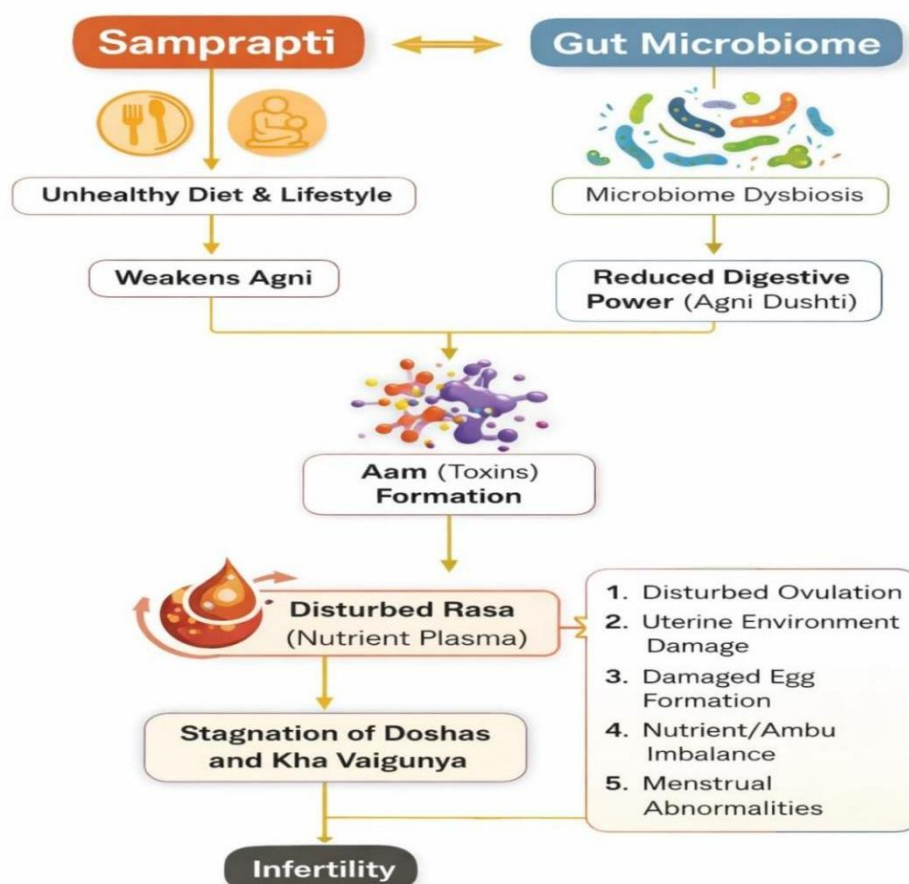


Fig. no. 1: Relationship between *Agni*, gut microbiota and infertility.

*Jatharagni*, responsible for breaking down food into assimilable nutrients, when weakened, produces improper *Aadya Rasa Dhatu* from *Aahara Rasa*. This causes *Tridosha Prakopa* and formation of *Aamvisha* that is a toxic state comparable to microbial endotoxins in modern science. *Aamvisha* reduces beneficial gut flora or leaky gut, causes *Sroto-avrodha* (channel obstruction), and vitiates *Dhatus*, leading to improper nourishment. Weak *Dhatvagni*, which governs nutrient assimilation across tissues, results in *Dhatu-kshaya*, particularly affecting *Aartava Dhatu* and *Uttroptar Dhatu* ultimately upto *Sukra Dhatu*, culminating in infertility. In Ayurveda, *Agni* (digestive fire) governs metabolic transformation; its impairment (*Mandagni*) initiates *Aam*

accumulation, obstructing *Aartavavaha Srotas* and leading to disorders such as PCOS, irregular menstruation, PMS, and infertility.

From a translational perspective, *Agni* and gut microbiota represent convergent paradigms of metabolic integrity. A balanced gut flora enhances estrogen recycling, insulin sensitivity, and immune modulation, while robust *Agni* ensures proper digestion, assimilation, and transformation into *Oja* that is the vital essence supporting reproductive vitality. Conversely, weakened *Agni* and microbial imbalance foster systemic inflammation and hormonal instability, mirroring the pathophysiology described in Ayurvedic Samprapti.

**Table 1: Conceptual Correlations Between Agni, Gut Microbiota, and Female Infertility.**

| Ayurvedic Concept       | Description in Ayurveda                                                                                                                    | Gut Microbiota Correlation                                                                                                 | Potential Impact on Female Fertility                                    |
|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| <i>Sama Agni</i>        | Balanced digestive and metabolic function                                                                                                  | healthy microbial diversity and stability                                                                                  | Supports hormonal balance, nutrient absorption, and reproductive health |
| <i>Agni impairment</i>  | <i>Agnivaishamyta</i>                                                                                                                      | Gut dysbiosis                                                                                                              | Reproductive dysfunction, nutrition hampered                            |
| <i>Aam</i>              | Improper <i>Paka</i> of <i>Aahara</i> causes <i>Rasadushti</i> and <i>Aamvisha</i> formation                                               | Dysbiosis-associated endotoxins, lipopolysaccharides (LPS), inflammatory metabolites causes chronic low-grade inflammation | Systemic inflammation, impaired implantation, reproductive dysfunction  |
| <i>Aartavadushti</i>    | <i>Aartavavaha Srotas</i> obstruction causes <i>Aartavadushti</i> like menstrual irregularities( <i>Anartava</i> , <i>Alapartava</i> etc.) | Gut microbiota regulates estrogen metabolism through estrobolome                                                           | Altered Menstrual health, ovulation, decreased fertility potential      |
| <i>Srotorodha</i>       | Obstruction of body channels                                                                                                               | Gut barrier dysfunction, endotoxins in blood and metabolic disturbances                                                    | Altered hormone transport and reproductive dysfunction                  |
| <i>Dhatu Agnimandya</i> | It causes reduced <i>Dhatupushti</i> leading to <i>Dhatukshya</i>                                                                          | Altered nutrient metabolism                                                                                                | Poor <i>Bija</i> quality                                                |

Dietary regulation and inclusion of probiotic rich foods such as fermented preparations analogous to Ayurvedic *Takra* or *Kanji* restore microbial diversity and digestive strength, this is indicated in *Mandagni*.<sup>[17]</sup> Therapeutic interventions like Panchakarma, particularly *Virechana* and *Basti* detoxify the gut, balance *Doshas*, and rejuvenate reproductive tissues.

Thus, integrating Ayurvedic principles of *Agni* and *Aam* with modern gut microbiome physiology offers a holistic framework for understanding infertility. This conceptual synthesis emphasizes that maintaining *Agni* and microbial equilibrium is fundamental to reproductive health, bridging traditional wisdom with contemporary biomedical science.

## CONCLUSION

This conceptual review highlights a strong conceptual correlation between *Agni* and *Aam* in Ayurveda and gut microbiota in modern science. Both systems emphasize digestive and metabolic integrity as the foundation of reproductive health. Integrative strategies combining Ayurvedic dietary and lifestyle modifications with

microbiome based therapies may provide novel preventive and therapeutic avenues for infertility. In Ayurveda, impaired *Agni* leads to the formation of *Aam*, obstruction of *Srotas*, and *Dhatuskshaya*, culminating in infertility. Modern biomedical science similarly demonstrates that gut dysbiosis disrupts estrogen metabolism, insulin sensitivity, and immune homeostasis, contributing to conditions such as PCOS, menstrual irregularities, endometriosis, and infertility.

Future research should focus on clinical validation of integrative models, exploring how modulation of gut microbiota alongside strengthening of *Agni* can optimize fertility outcomes. This synthesis bridges traditional wisdom with contemporary biomedical science, offering a holistic paradigm for reproductive health.

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