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Beyond the Ovary: Integrating the Gut-Ovary Axis with Grahani and Artavavaha Srotas in Polycystic Metabolic Ovarian Disease (PMOD): A Narrative Review

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ABSTRACT:
Polycystic Metabolic Ovarian Disease (PMOD), formerly known as Polycystic Ovary Syndrome (PCOS), is a complex endocrine-metabolic disorder characterized by reproductive, hormonal, and metabolic abnormalities. Recent evidence suggests that PMOD is not merely an ovarian disease but a systemic disorder involving intricate interactions among insulin resistance, chronic inflammation, oxidative stress, and gut microbiota dysbiosis. The emerging concept of the gut ovary axis highlights the influence of intestinal microbial homeostasis on endocrine regulation, ovarian function, and female fertility. Although PMOD is not described as a distinct disease entity in *Ayurved*, its clinical manifestations can be understood through the concepts of *Grahani Dushti, Agnimandya, Ama, Kapha - Meda dushti,* and *Artavavaha Srotodushti*. Disturbance of *Grahani* initiates metabolic dysfunction, leading to *Ama* formation and *Srotorodha*, which ultimately affect *Artava* and reproductive health. These concepts exhibit remarkable similarities to the modern understanding of gut dysbiosis and metabolic inflammation. This narrative review explores the current evidence on the gut-ovary axis in PMOD and critically correlates it with classical *Ayurvedic* principles to provide an integrative understanding of disease pathogenesis. The review also highlights the potential role of gut microbiota modulation, lifestyle modification, and *Ayurvedic* interventions in improving metabolic and reproductive outcomes, thereby offering a holistic framework for future research and personalized management of PMOD.

KEYWORDS: *Artavavaha Srotas*, *Ayurveda*, *Grahani*, Gut-Ovary Axis, Insulin Resistance, PMOD.

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INTRODUCTION:

Polycystic Metabolic Ovarian Disease (PMOD), formerly known as Polycystic Ovary Syndrome (PCOS), is one of the most common endocrine-metabolic disorders affecting women of reproductive age worldwide. The disorder is characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, frequently accompanied by insulin resistance, obesity, dyslipidemia, and chronic low-grade inflammation. [1] Beyond reproductive dysfunction, PMOD is associated with significant metabolic and psychological consequences, including type 2 diabetes mellitus, metabolic syndrome, cardiovascular risk, infertility, anxiety, and depression. [2]

Recent advances have shifted the understanding of PMOD from an isolated ovarian disorder to a systemic metabolic disease. Among the emerging concepts, the gut ovary axis has gained considerable attention because alterations in gut microbial composition can influence immune responses, insulin sensitivity, steroid hormone metabolism, and ovarian physiology. Gut dysbiosis has therefore emerged as a potential contributor to the initiation and progression of PMOD. [3]

Ayurved does not describe PMOD as an individual disease; however, its clinical presentation closely resembles disorders involving *Artavakshaya, Vandhyatva, Pushpaghni Jataharini,* and *Artavavaha Srotodushti.* The *Ayurvedic* concept of *Grahani,* the seat of *Agni,* plays a pivotal role in maintaining digestion, metabolism, and tissue nourishment. Disturbance of *Grahani* results in *Agnimandya, Ama* formation, and *Srotorodha,* ultimately impairing *Artava* and reproductive function. This conceptual similarity provides a scientific basis for integrating the gut-ovary axis with the *Ayurvedic* understanding of PMOD.

The functional efficiency of *Grahani* depends upon *Agni*(digestive fire) and *Agniis* the seated within *Grahani* itself thus *Agni* and *Grahani* maintain the close interdependent relationship in the process of digestion and metabolism. Hence, when the *Vahni* (digestive fire) is vitiated, *Grahani* also becomes vitiated. [4] Functionally weak *Agni* i.e., *Mandagni*, causes improper digestion of ingested food, which leads to *Ama Dosha*. This *Ama Dosha* is a root cause of most of the diseases. It has pivotal importance in the pathogenesis of *Grahani Roga. Grahani* is considered under eight major diseases, [5] hence it is hard to diagnose and difficult to treat. Any disease has two

stages: *Amavastha* and *Niramavastha*. If the disease is in *Amavastha*, first line of the treatment is to remove *Ama* and make the disease *Nirama*, and then after that the particular treatment of the disease should be applied.

The present review aims to explore the emerging role of the gut- ovary axis in PMOD and correlate contemporary biomedical evidence with the *Ayurvedic* concepts of *Grahani* and *Artavavaha Srotas* to develop an integrative understanding of disease pathogenesis and management.

The Gut - Ovary Axis: An Emerging Paradigm in PMOD

The human gastrointestinal tract harbors a diverse microbial community that plays a vital role in regulating metabolism, immune homeostasis, nutrient absorption, and endocrine function. Recent evidence has established that alterations in gut microbiota composition, collectively termed gut dysbiosis, are closely associated with the development and progression of Polycystic Metabolic Ovarian Disease (PMOD). [6]

Women with PMOD exhibit reduced microbial diversity, depletion of beneficial bacteria, and increased abundance of pro-inflammatory microorganisms. These alterations impair the production of short-chain fatty acids (SCFAs), including butyrate, acetate, and propionate, which are essential for maintaining intestinal barrier integrity, glucose metabolism, and insulin sensitivity. Reduced SCFA production contributes to increased intestinal permeability ("leaky gut"), facilitating the translocation of bacterial lipopolysaccharides into the systemic circulation. [7]

Circulating LPS activates inflammatory pathways through toll-like receptor-4 (TLR4), leading to chronic low-grade inflammation and insulin resistance. Hyperinsulinemia subsequently stimulates ovarian theca cells to produce excess androgens while reducing hepatic synthesis of sex hormone-binding globulin (SHBG), resulting in hyperandrogenism, follicular arrest, anovulation, and infertility. In addition, gut microbiota influences bile acid metabolism and neuroendocrine signaling, thereby regulating the hypothalamic-pituitary-ovarian axis and ovarian steroidogenesis. [8]

These findings suggest that PMOD should be regarded as a disorder of the gut-metabolism-ovary axis rather than an isolated ovarian disease. Consequently, interventions targeting gut microbial homeostasis, including dietary modification, increased dietary fibre intake, probiotics, prebiotics, and healthy lifestyle practices, are emerging as promising adjunctive strategies for improving metabolic and reproductive outcomes in women with PMOD. [9]

Gut - Brain - Ovary Neuroendocrine Pathway

The interaction between the gut and the central nervous system is referred to as the gut - brain axis, and recent studies have found that this pathway is also important in regulating reproductive function. Gut microbiota can influence the activity of gonadotropin-releasing hormone (GnRH) neurons through the vagus nerve or serotonin pathways, thereby modulating the function of the hypothalamic-pituitary-ovarian (HPO) axis.

Research shows that gut microbiota can affect ovarian function by modulating neuroendocrine signals and subsequently influence menstrual cycles and ovulation. [10] This gut-brain-ovary neuroendocrine pathway suggests that changes in gut microbiota may influence the synthesis and secretion of ovarian hormones by affecting GnRH release, providing a new perspective on the pathogenesis of PMOD and related reproductive endocrine disorders.

Therefore, interventions targeting gut microbiota may become effective strategies for regulating this pathway and improving PMOD symptoms. [Figure 1]

Modern Pathophysiology of PMOD

Polycystic Metabolic Ovarian Disease (PMOD) is a multifactorial endocrine metabolic disorder resulting from the interaction of genetic susceptibility, environmental factors, hormonal imbalance, and metabolic dysfunction. Insulin resistance is considered the central pathogenic mechanism and is present in nearly 70–80% of affected women. Compensatory hyperinsulinemia stimulates ovarian theca cells to produce excess androgens while suppressing hepatic sex hormone-binding globulin (SHBG), resulting in hyperandrogenism, follicular arrest, and chronic anovulation.

Persistent insulin resistance is further aggravated by chronic low-grade inflammation, oxidative stress, obesity, and adipokine imbalance, creating a vicious cycle between metabolic and reproductive dysfunction. Recent evidence also indicates that gut dysbiosis amplifies these abnormalities through increased intestinal permeability, endotoxemia, and altered microbial metabolites, linking gut health with ovarian physiology. [11]

Although ovarian dysfunction is the primary clinical manifestation, PMOD is now recognized as a systemic metabolic disorder involving multiple organs, including the gut, liver, adipose tissue, pancreas, and ovary. This integrated understanding has shifted the focus from symptom management to correction of the underlying metabolic disturbances. [12] [Table 1] [Figure 1]

Table- 1: Major Modern Pathophysiological Mechanisms in PMOD

Mechanism	**Clinical consequence**
Insulin resistance	Hyperinsulinemia, hyperandrogenism
Chronic inflammation	Cytokine activation, ovarian dysfunction
Oxidative stress	Poor oocyte quality
Adipokine imbalance	Obesity, metabolic syndrome
Gut dysbiosis	Leaky gut, endotoxemia, insulin resistance

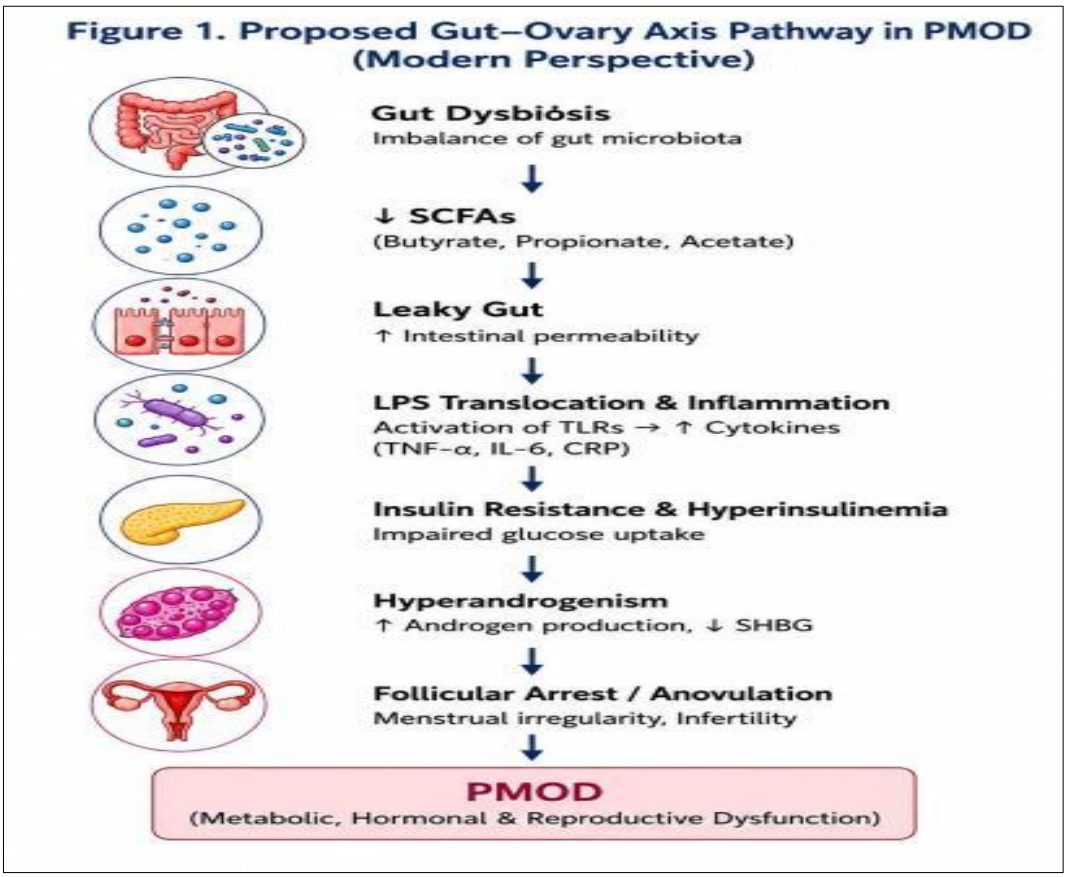


FIGURE 1- GUT-OVARY AXIS IN PMOD- PATHWAY

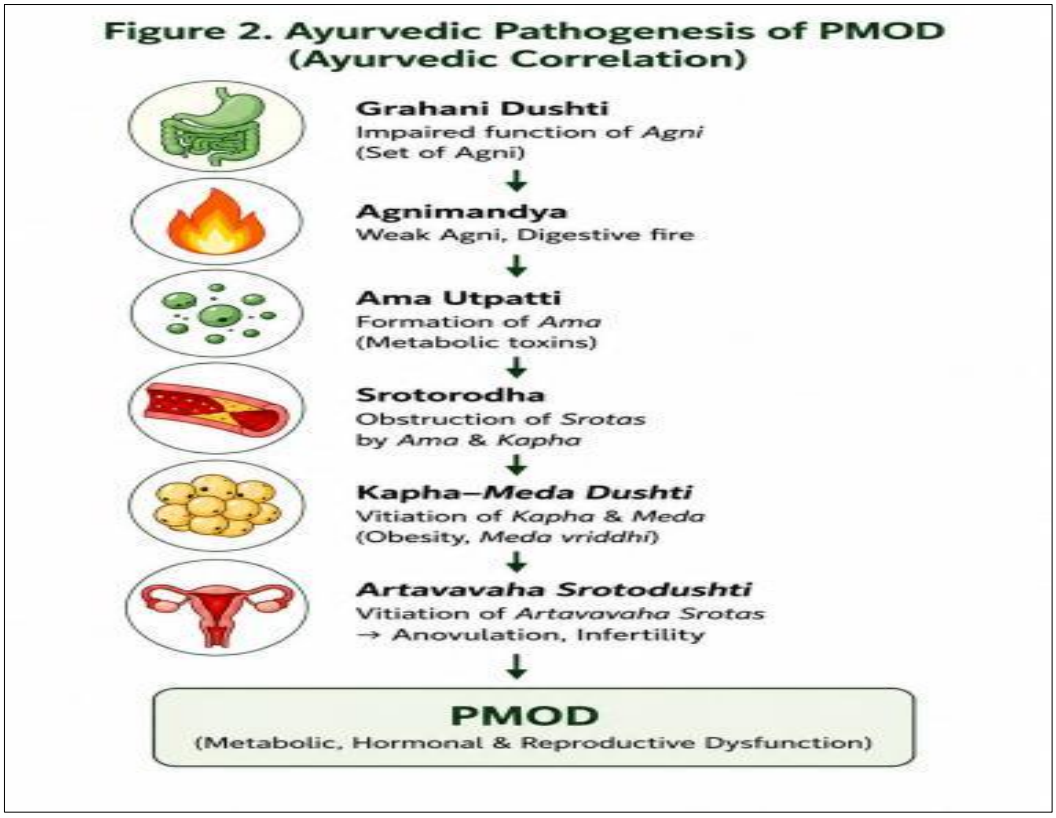


FIGURE 2- AYURVEDIC PATHOGENESIS OF PMOD

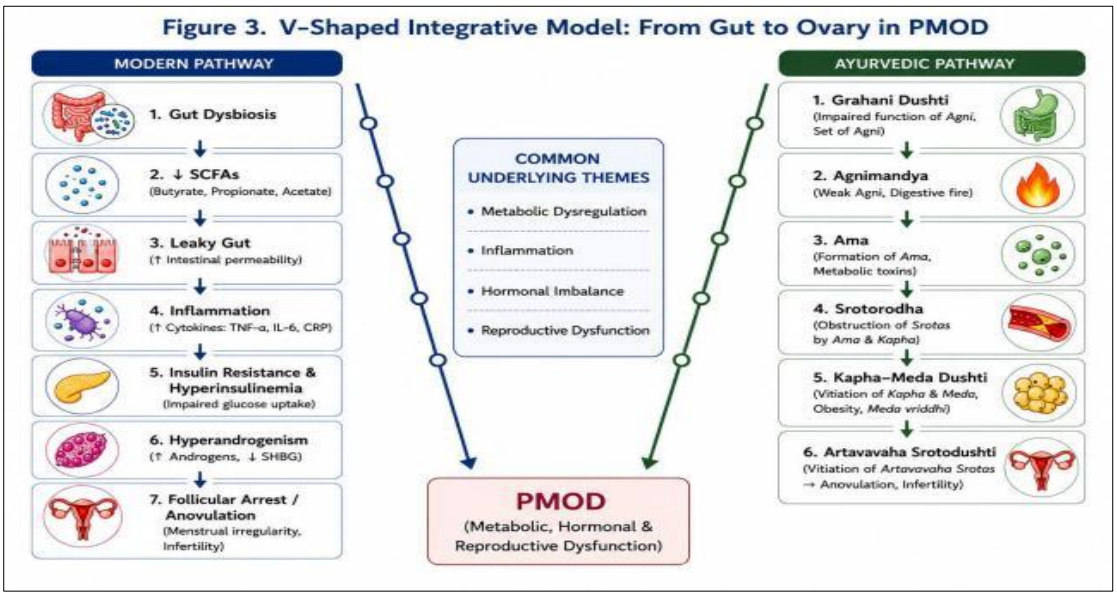


FIGURE 3- MODERN - AYURVEDIC CORRELATION IN PMOD

***Ayurvedic* Perspective of PMOD: *Grahani* as the Central Pathogenic Link**

Artavavaha Srotas plays an important role in female reproductive physiology and is closely related to the structures and functions of the female reproductive system. Disturbance or injury to *Artavavaha Srotas* is described in association with *Artavanasha* and *Vandhyatva.* Therefore, dysfunction of *Artavavaha Srotas* may be considered relevant while interpreting menstrual irregularity, anovulation, and infertility in Polycystic Metabolic Ovarian Disease (PMOD). [13] Rather than considering ovarian dysfunction as the primary pathology, *Ayurved* emphasizes that disease originates from disturbed digestion and metabolism. Thus, *Grahani* emerges as the central pathological link in understanding PMOD. [14]

Grahani, regarded as the seat of *Agni*, is responsible for digestion, absorption, transformation, and assimilation of nutrients. Impairment of *Grahani* leads to *Agnimandya,* resulting in incomplete digestion and the formation of *Ama*. *Ama,* being metabolically toxic and obstructive in nature, initiates *Srotorodha,* particularly affecting *Medovaha* and *Artavavaha Srotas.* Consequently, *Kapha* and *Meda* become vitiated, disturbing normal *Artava* formation, follicular maturation, and ovulation.

The metabolic abnormalities observed in PMOD, including obesity, insulin resistance, chronic inflammation, and reproductive dysfunction, closely resemble the *Ayurvedic* sequence of *Grahani Dushti* → *Agnimandya* → *Ama* → *Srotorodha* → *Kapha-Meda Dushti* → *Artavavaha Srotodushti.* This correlation suggests that restoration of *Agni*, elimination of *Ama,* and normalization of *Srotas* are fundamental therapeutic principles in the *Ayurvedic* management of PMOD. [15]

By symptoms and signs of Polycystic Metabolic Ovarian Disease (PMOD), we can consider it as *Kapha-Vata*

Predominant *Tridhoshaj ArtavaDushti.* As *Vata* is responsible for the division of cells (granulosa, theca cells), rupture of the follicle, etc. *Pitta* has *paaka karma* associated with the conversion of androgen to estrogen & maturity of follicles. Subsequently, due to its *Shrava Karma*, it results in ovulation with the help of *Vata*. *Kapha* has a nutritive function along with *Vata* helps in the proliferation of ovarian follicles. Although in *Ayurved* description of PMOD is as such not present but to some extent few diseases simulated as described by some Scholars-

1. *Pushpaghani Jataharni-* "*vrutha pushpam" & "sthula Loma gandasha*" [16]: Menses occurs regularly at the usual time and the women suffering from this type of infertility have obese cheeks covered with hairs. Description of obese cheeks may indicate central obesity which is found in PMOD as steroid hormones, mainly androgen have increased. Also, there is an indication of hirsutism, which is again due to androgen excess. The name *Phuspaghani* here indicates, infertility due to anovulation or due to the formation of bad quality of ovum or defective endometrium.

2. *Vikuta Jataharni-* Menses are irregular in terms of duration, color, and amount. In the anovulatory and oligo-ovulatory cycle menses are either scanty or excessive in terms of amount either there is oligomenorrhoea or amenorrhea. Menses may vary in duration of bleeding and color, according to the interval at which menstrual bleeding starts. It seems to be due to oligo ovulation or anovulation found in PMOD.

3. *Artavakshaya*- *"yatho uchita kalam aadarshanam alptaa va yoni vedana cha"*: In *Artava kshya* there are features of oligomenorrhea, scanty menses, and painful menses explains PMOD only partially. Since *acharyas* mainly focused on the description of *Bahaya Atarva Lakshana* (menstrual blood) not the other, signs of androgen excess and the presence of cystic ovaries have not been explained. [17]

4. *Granthibhut artava dushti* [18]- As *Artava* word used for an ovum, hormone, and menstrual blood. We see in *beeja roopiartava*/ovum is anovulation cystic ovaries if we consider that the *Antaha Artava*/hormones get vitiated by excess *Kapha* and *Vata* and the *Bahaya Artava*/ menstrual blood will also form clots, either with the scanty or heavy flow depending on *dosha* predominance. Or there may be hyperplasia of the endometrium from polyps. In the *Nidana* of *Nasta artava, Acharya Vagbhata* has explained that due to obstruction of channels *Artava* is not evident, the patient remains amenorrheic. All these facts indicate that *Vata-Kapha Dosha* predominance in this disorder and symptoms appear according to predominance between two *doshas*. But if we closely look at symptoms & signs of PMOD.
Pushpaghani jataharini described by *Acharya Kashyapa* seems to be closer to symptoms & signs of PMOD.

✓*Vratha pushpam*- The ovum or prepared endometrium is not useful for conception. ✓*Stulalomagandasha*- The patient having chubby or fatty cheeks with excessive hair growth. [Figure 2]

Bridging Lifestyle, Diet, *Agni, Dhatvagni*, and *Dhatu* Formation

Improper lifestyle *(Vihara)* and dietary patterns *(Ahara)* such as excessive intake of *Guru, Snigdha, Madhura* foods, irregular meals, sedentary habits, and stress lead to *Agni* impairment at the *Jatharagni* level. This results in *Grahani* dysfunction, which subsequently alters *Dhatvagni* function across all seven *Dhatus.*

Rasa Dhatu* and *Artava* as *Upadhatu

In females, *Artava* (menstrual blood and ovum) is the *Upadhatu* of *Rasa Dhatu,* formed over approximately one month from properly digested *Ahara Rasa*. When *Rasagni* is impaired due to *Ama* and *Srotorodha, Rasa Dhatu* formation becomes inadequate or vitiated *(Rasa Dushti)*, leading to defective *Artava* formation. [19]

This explains anovulation and menstrual irregularity in Polycystic Metabolic Ovarian Disease (PMOD) as consequences of:

Rasa Kshaya or *Rasa Dushti* → *Artava Kshaya/Dushti* → Anovulation and irregular menstruation.

***Meda Dhatu* and *Dhatvagni* Involvement**

In Polycystic Metabolic Ovarian Disease (PMOD), *Meda Dhatu* accumulation (obesity, insulin resistance) reflects *Medagni Mandya* and *Kapha-Meda Dushti.* [20] Excess *Meda* further obstructs *Artavavaha Srotas,* compounding reproductive dysfunction.

***Mala* Formation and Clinical Correlates**

Excessive or abnormal *Mala* formation is another consequence of impaired *Agni* and *Dhatvagni. Kesha* and *Loma* are *Malas* of *Asthi Dhatu*; their abnormal growth (e.g., hirsutism) in PMOD can be interpreted as a manifestation of Asthi Dhatu involvement secondary to *Kapha-Vata* vitiation and *Meda Dushti.* [21]

Proposed *Ayurvedic Samprapti* for Polycystic Metabolic Ovarian Disease (PMOD)

Nidana (Lifestyle & Dietary Factors) → *Agni* Impairment (*Jatharagni Mandya*) → *Grahani* Dysfunction → *Ama* Formation & Srotorodha → Altered *Dhatvagni* (*Rasagni, Medagni,* etc.)

→ Improper *Dhatu* Formation *(Rasa Kshaya/Dushti, Meda Vriddhi)* → Abnormal *Mala* Formation *(Kesha/Loma Vriddhi)* → Impaired *Rasa-Artava* Relationship → *Artavavaha Srotodushti* → Menstrual Irregularity / Anovulation (PMOD).

Integrative Perspective: Gut-Ovary Axis and *Grahani*

Contemporary research identifies **gut dysbiosis** as an initiating factor that disrupts intestinal homeostasis, promotes chronic inflammation, and induces insulin resistance, ultimately impairing ovarian function. In *Ayurved*, a comparable sequence begins with ***Grahani Dushti***, where impaired *Agni* leads to ***Ama*** formation and

Srotorodha, resulting in metabolic and reproductive dysfunction.

- Reduced **SCFAs** and increased intestinal permeability ("leaky gut") promote systemic endotoxemia- paralleling ***Ama*** obstructing ***Srotas***.
- Chronic insulin resistance and obesity correlate with ***Kapha-Meda Dushti***.
- Ovarian dysfunction and anovulation resemble ***Artavavaha Srotodushti***.

These similarities suggest that Polycystic Metabolic Ovarian Disease (PMOD) should be understood as a disorder originating from **metabolic dysregulation** rather than an isolated ovarian disease. An integrative therapeutic approach aimed at restoring gut health, improving metabolic function, correcting *Agni*, eliminating *Ama*, and maintaining the integrity of *Artavavaha Srotas* may provide a more comprehensive strategy for improving reproductive and metabolic outcomes. [Figure 3]

Future Perspectives:

Growing evidence suggests that Polycystic Metabolic Ovarian Disease (PMOD) management should extend beyond hormonal regulation and include restoration of metabolic and gut homeostasis. Advances in microbiome research have identified dietary interventions, probiotics, prebiotics, synbiotics, and microbiota-targeted therapies as promising adjuncts for improving insulin sensitivity and reproductive function. Similarly, *Ayurvedic* principles focusing on *Agni Deepana, Ama Pachana, Srotoshodhana,* and lifestyle modification may complement conventional treatment by addressing the underlying metabolic disturbances. Future multidisciplinary studies integrating microbiome science with *Ayurvedic* concepts are needed to validate these correlations and develop evidence-based personalized management strategies.

CONCLUSION:

Polycystic Metabolic Ovarian Disease (PMOD) is now recognized as a systemic metabolic disorder rather than an isolated ovarian disease. Emerging evidence highlights the gut-ovary axis as a critical link between gut dysbiosis, insulin resistance, chronic inflammation, and ovarian dysfunction. The *Ayurvedic* concepts of *Grahani Dushti, Agnimandya, Ama, Kapha-Meda Dushti,* and *Artavavaha Srotodushti* closely parallel these metabolic alterations, providing a holistic framework for understanding disease pathogenesis. Integrating contemporary biomedical evidence with *Ayurvedic* principles may facilitate early intervention, personalized management, and improved reproductive and metabolic outcomes in women with PMOD. Further clinical and translational research is warranted to validate this integrative model.

Limitation of study: This narrative review is limited by the lack of systematic literature search and quantitative analysis. The proposed correlations between the gut-ovary axis and Ayurvedic concepts are primarily conceptual and are supported by limited clinical evidence. Variations in diagnostic criteria, study design, and therapeutic protocols may also restrict

the generalizability of the findings. Therefore, well-designed clinical and translational studies are required to validate these integrative correlations.

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Guarantor*:* The corresponding author is the guarantor of this article and its contents.

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