



Exploring Gut-Related Symptom Patterns Across Different Mizaj Profiles of Polyendocrine Metabolic Ovarian Syndrome (PMOS): A Preliminary Unani Clinical Case Series

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Orcid Id: 0009-0009-5362-5032

OPEN ACCESS

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Received: 09-11-2025

Accepted: 20-12-2025

Published: 01-01-2026

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ABSTRACT

Background: Polyendocrine Metabolic Ovarian Syndrome (PMOS), formerly termed polycystic ovary syndrome, is a heterogeneous endocrine-metabolic disorder frequently associated with menstrual, metabolic, and gastrointestinal manifestations. In Unani medicine, constitutional variation is characterized through Mizaj, which may influence differences in clinical presentation. This preliminary study explored gut-related symptom patterns across different Mizaj profiles in women with PMOS.

Methods: A preliminary longitudinal clinical case series included 20 women aged 18–40 years with a previously documented diagnosis of PCOS/PMOS. Participants were classified into four Mizaj categories: Damvi, Balghami, Safravi, and Saudawi, with five participants in each group. Baseline assessment included menstrual history, PMOS-related manifestations, gastrointestinal symptoms, Mizaj profile, available ultrasonographic findings, and laboratory investigations.

Results: Gastrointestinal manifestations varied across Mizaj profiles. Bloating was observed across all four groups. Damvi participants predominantly presented with abdominal bloating and fullness, whereas Balghami participants showed constipation, bloating, sluggish digestion, and flatulence. Safravi participants demonstrated bloating, dyspeptic symptoms, and altered bowel habits, while Saudawi participants predominantly showed constipation, abdominal discomfort, bloating, and flatulence.

Conclusion: Women with PMOS demonstrated distinct patterns of gastrointestinal and menstrual symptoms across different Mizaj profiles.

Keywords: Polyendocrine Metabolic Ovarian Syndrome; PMOS; polycystic ovary syndrome; Mizaj; Unani medicine; gastrointestinal symptoms; constipation; bloating; menstrual irregularity.

INTRODUCTION

Polyendocrine metabolic ovarian syndrome (PMOS), formerly known as polycystic ovary syndrome (PCOS), is a common, heterogeneous and lifelong endocrine-metabolic disorder affecting women of reproductive age. In 2026, an international multistep consensus process formally proposed the term PMOS to replace PCOS because the traditional name placed disproportionate emphasis on ovarian morphology and did not adequately represent the broader endocrine, metabolic and multisystem manifestations of the condition [1]. PMOS is estimated to affect approximately one in eight women worldwide and is characterized by varying combinations of ovulatory dysfunction, androgen excess and altered ovarian morphology, frequently accompanied by insulin resistance, adiposity, dyslipidaemia and other metabolic abnormalities [1]. Current evidence-based recommendations emphasize that the clinical expression of the syndrome varies substantially among affected women and that assessment should extend beyond reproductive manifestations to metabolic, psychological and long-term health consequences [2]. This phenotypic heterogeneity provides a strong rationale for investigating symptom patterns that may not be captured adequately by conventional reproductive and biochemical classifications.

The burden of PMOS is particularly relevant in India, where differences in lifestyle, dietary habits, body composition, genetic susceptibility and environmental exposures may influence its clinical presentation. A systematic review and meta-analysis of Indian studies reported a pooled PCOS prevalence of approximately 11.33%, although prevalence estimates

differed according to the diagnostic criteria employed [3]. Beyond menstrual irregularity, infertility, hirsutism, acne and weight-related concerns, women with PMOS can experience symptoms involving multiple organ systems. Gastrointestinal complaints, although comparatively less emphasized in routine PMOS evaluation, may represent an important component of this wider symptom spectrum.

Evidence suggesting an association between PMOS and gastrointestinal dysfunction has gradually accumulated. Mathur et al. observed a markedly greater prevalence of irritable bowel syndrome (IBS) among women with PCOS than among controls, with IBS identified in 42% of the PCOS group compared with 10% of controls [4]. Such observations raise the possibility that symptoms including abdominal pain or discomfort, bloating, altered bowel frequency, constipation and diarrhoeal tendencies may occur alongside the reproductive and metabolic manifestations of PMOS. However, gastrointestinal symptoms have not been systematically incorporated into routine clinical phenotyping, and considerable individual variability is likely.

Interest in the gut–ovary and gut–metabolic axes has further strengthened the biological rationale for examining gastrointestinal manifestations in PMOS. Studies assessing the intestinal microbiome have demonstrated differences in microbial diversity and composition in subsets of women with the syndrome. Torres et al. reported reduced gut microbial alpha diversity in women with PCOS and demonstrated associations between microbial diversity, hyperandrogenism, serum testosterone and hirsutism [5]. Mechanistic work has additionally suggested interactions among intestinal microorganisms, bile-acid metabolism, immune signalling, insulin resistance and ovarian dysfunction. Qi et al. demonstrated alterations in gut microbial composition and bile-acid metabolism and proposed a microbiota–bile acid–interleukin-22 pathway capable of influencing metabolic and reproductive abnormalities associated with PCOS [6]. These findings support the concept that the gastrointestinal environment may interact with the endocrine and metabolic disturbances underlying PMOS rather than functioning merely as an unrelated source of symptoms.

Nevertheless, the relationship is not uniform, and available evidence should be interpreted cautiously. In a case-control investigation of gastrointestinal permeability and dysbiosis markers, Lingaiah et al. found no significant overall differences in zonulin, fatty acid-binding protein-2 or urinary indican between women with PCOS and body mass index-matched controls. Importantly, some gastrointestinal markers were associated with obesity, insulin resistance and inflammatory indices, suggesting that metabolic status itself may contribute substantially to gut-related abnormalities [7]. Therefore, PMOS-related gastrointestinal symptoms are likely to reflect a complex interaction of metabolic state, dietary exposures, hormonal alterations, intestinal function and individual susceptibility rather than a single universal gastrointestinal phenotype.

Such individual variation is particularly relevant to the Unani concept of Mizaj (temperament). Mizaj is a fundamental principle of Unani medicine used to describe an individual's constitutional and functional characteristics in relation to qualitative attributes such as hotness, coldness, moistness and dryness. Conventional Mizaj profiles include *Damawi* (sanguine), *Safrawi* (choleric), *Balghami* (phlegmatic) and *Saudawi* (melancholic), representing different combinations of these qualities. In Unani theory, maintenance of an individual's characteristic temperament contributes to physiological equilibrium, whereas disturbance or *Su'-i-Mizaj* is considered relevant to susceptibility to disease and differences in clinical expression [8]. A clinical study conducted at the National Institute of Unani Medicine, Bengaluru, demonstrated the feasibility of categorizing patients according to Mizaj and investigating associations between temperament and disease patterns [8].

Contemporary research has also attempted to improve the objectivity and reproducibility of Mizaj assessment. Mojahedi et al. developed and evaluated a self-report Mizaj questionnaire capable of differentiating individuals along hot–cold and wet–dry dimensions, providing a methodological basis for incorporating temperament assessment into clinical research [9]. Although Mizaj should not be considered biologically synonymous with contemporary concepts such as metabolic phenotype, intestinal microbiota composition or gut permeability, it may serve as a traditional individualized framework through which variation in symptom expression can be explored.

The possible relevance of temperament to ovarian disorders has recently received greater attention. Nazmi et al., in a case-control study involving women with and without PCOS, reported that cold uterine temperament was significantly more frequent among women with PCOS, although differences in overall body temperament were less pronounced [10]. These observations suggest that temperament-based assessment may identify clinically meaningful subgroups and justify further investigation of Mizaj in women with PMOS. However, evidence specifically linking different Mizaj profiles with gastrointestinal symptom patterns in PMOS remains extremely limited.

Considering the emerging recognition of PMOS as a multisystem endocrine-metabolic disorder, the growing evidence for gut-related involvement, and the individualized framework provided by Unani Mizaj, exploration of gastrointestinal symptom patterns across different temperament profiles represents a potentially useful area of clinical inquiry. A preliminary clinical case-series approach may help identify whether symptoms such as bloating, abdominal discomfort, altered appetite, constipation, loose stools, dyspeptic complaints or other gut-related manifestations tend to cluster within particular Mizaj profiles. Such observations should be considered hypothesis-generating rather than evidence of causal relationships between Mizaj and gastrointestinal pathophysiology. Accordingly, the present preliminary Unani clinical case series aims to explore the distribution and patterns of gut-related symptoms across different Mizaj profiles among women

with PMOS and to identify potential temperament-specific symptom clusters that may inform subsequent larger, systematically designed clinical studies.

MATERIALS AND METHODS

Study Design

This study was designed as a preliminary longitudinal clinical case series to explore gut-related symptom patterns across different Mizaj profiles among women with Polyendocrine Metabolic Ovarian Syndrome (PMOS), historically diagnosed as polycystic ovary syndrome (PCOS), and to document changes in gastrointestinal and menstrual symptoms following individualized Mizaj-based Unani management.

The study was conducted in the outpatient department of Regional Research Institute of Unani Medicine Mumbai, Maharashtra, India, during **January 2023 – December 2023**. Because the primary purpose of this preliminary case series was exploratory and hypothesis-generating, the study focused principally on detailed clinical characterization and descriptive comparison of symptom patterns rather than formal testing of causal associations.

Study Population

A total of 20 women aged 18–40 years with a previously documented diagnosis of PCOS, referred to as PMOS in the present study, were included. All participants were evaluated in the Unani outpatient setting and underwent systematic baseline assessment of menstrual, gastrointestinal, metabolic and constitutional characteristics.

Participants were classified according to their predominant Mizaj into four groups:

- Damvi: n = 5
- Balghami: n = 5
- Safravi: n = 5
- Saudawi: n = 5

Thus, each Mizaj category consisted of five participants, allowing descriptive comparison of clinical and gastrointestinal symptom patterns across the four constitutional profiles.

Eligibility Criteria

Women were eligible for inclusion when they were:

1. aged between 18 and 40 years;
2. previously diagnosed with PCOS/PMOS and attending the study outpatient department;
3. clinically assessed for menstrual, gastrointestinal and Mizaj-related characteristics at baseline;
4. available for treatment and subsequent clinical follow-up; and
5. willing to participate and provide written informed consent.

Clinical Data Collection

Clinical information was documented at baseline using a structured case-record format. Recorded variables included age, menstrual history, gastrointestinal complaints, clinical manifestations related to PMOS, Mizaj category, available pelvic ultrasonography findings and relevant biochemical investigations.

Particular attention was given to the coexistence of gastrointestinal and menstrual symptoms within each Mizaj profile. Clinical manifestations associated with PMOS, including weight gain, central adiposity, acne, hirsutism, altered appetite, lethargy and other documented metabolic or constitutional manifestations, were recorded when present.

Assessment of Menstrual Symptoms

A detailed menstrual history was obtained at baseline. The principal menstrual abnormalities documented included:

- irregular menstruation;
- oligomenorrhoeic or prolonged menstrual cycles;
- delayed menstruation;
- scanty menstrual bleeding; and
- other clinically relevant changes in menstrual pattern.

Where information was available, cycle interval, nature of menstrual disturbance and duration of the problem were recorded. Menstrual symptoms were reassessed after three months of treatment, and the follow-up pattern was compared descriptively with the baseline clinical presentation.

Assessment of Gastrointestinal Symptoms

Gut-related manifestations were systematically documented as part of the clinical evaluation. Symptoms of interest included:

- constipation;
- abdominal bloating;
- flatulence;
- dyspeptic symptoms;
- abdominal discomfort or fullness;

- sluggish digestion; and
- altered bowel habits.

For each participant, the presence or absence of individual gastrointestinal symptoms was recorded at baseline. Where symptom-severity information was available in the clinical record, baseline severity and change during follow-up were documented. Because this preliminary case series did not employ a validated gastrointestinal symptom questionnaire, gastrointestinal findings were interpreted as clinically observed symptom patterns rather than

Ultrasonographic Assessment

Available previous pelvic ultrasonography reports were reviewed as part of the baseline clinical documentation and to support the previously established diagnosis of PCOS/PMOS. When an adequate diagnostic ultrasonography report was already available, no additional imaging examination was performed solely for the purpose of the present clinical case series.

Ultrasonographic findings were therefore considered supportive clinical information rather than a study-specific imaging outcome.

Laboratory Investigations

Baseline laboratory assessment included:

- complete blood count (CBC);
- liver function tests (LFT);
- renal function tests (RFT); and
- serum prolactin.

Serum prolactin was evaluated as part of the baseline endocrine assessment. Liver and renal function tests were performed prior to initiation of treatment to establish baseline safety and were repeated following the intervention to assess potential treatment-related hepatic or renal abnormalities.

Available pre- and post-intervention CBC, LFT and RFT values remained within clinically acceptable limits.

Individualized Unani Intervention

Following clinical evaluation and Mizaj classification, participants received individualized Unani therapy according to their constitutional profile and predominant clinical manifestations. Four therapeutic regimens were employed.

Regimen 1 – Damvi profile

- Majoon Dabeed-ul-Ward: 10 g orally after breakfast with luke warm water
- Habbe Tinkar: 2 tab orally twice daily
- Sharbat Bazoori Motadil: 10 ml twice daily

Regimen 2 – Safravi profile

- Habbe Rasaut: 2 tab orally twice daily
- Itrifal Ustukhuddus: 10 g orally at bedtime with luke warm water
- Arq Brinjasaf: 10 mL orally twice daily before meal

Regimen 3 – Balghami profile

- Jawarish Zanjabeel: 5 g orally twice daily
- Arq Mako: 20 mL orally before meals
- Arq Kasni: 20 mL orally before meals

Regimen 4 – Saudawi profile

- Itrifal Gududi: 10 g orally at bedtime, with luke warm water
- Nankhwah, Badiyan and Waj Turki administered as a decoction (Joshanda), 6 g twice daily for 10 days, beginning five days before the expected menstrual period, for three consecutive months.

Each Regimen participant received Habbe Mudīr at a dose of two tablets twice daily (BD) for 5 consecutive days, initiated immediately prior to the expected onset of menstruation, after which the medication was discontinued.

Treatment selection was based on the participant's documented Mizaj and presenting clinical characteristics, consistent with the individualized therapeutic principle of Unani medicine. No attempt was made to compare the four regimens as equivalent pharmacological interventions because treatment assignment was constitution-based rather than randomized.

Lifestyle Intervention

Lifestyle modification was provided as an adjunct to the individualized Unani regimen for all participants. Standard advice included approximately 30 minutes of regular walking per day and restriction of junk food and foods high in fat or prepared by frying.

The lifestyle component was provided to all participants throughout the three-month intervention period and was therefore considered part of the overall clinical management rather than a separate experimental treatment arm.

Follow-up and Outcome Assessment

Participants were followed for three months after initiation of individualized Unani management. At the end of the follow-up period, menstrual and gastrointestinal symptoms were reassessed using the same clinical domains documented at baseline.

The principal clinical outcomes were:

1. change in individual gut-related symptoms;
2. overall pattern of gastrointestinal symptom response;
3. change in menstrual irregularities;
4. menstrual pattern at follow-up; and
5. occurrence of any treatment-related adverse clinical or laboratory findings.

Other relevant PMOS-associated manifestations were reassessed when information was available. Repeat investigations were documented when performed as part of routine clinical management or when clinically indicated.

Clinical response was categorized descriptively according to the documented change between baseline and follow-up. Given the exploratory design, improvement was interpreted as an observed clinical response rather than proof of treatment efficacy.

Primary and Secondary Outcomes

The primary outcome was the descriptive pattern and change of gut-related symptoms following three months of Mizaj-based individualized Unani management.

The principal gastrointestinal symptoms evaluated were constipation, bloating, flatulence, dyspepsia, abdominal discomfort/fullness and altered bowel habits.

The secondary outcomes included:

- distribution of gastrointestinal symptoms across the four Mizaj categories;
- baseline menstrual symptom patterns;
- change in menstrual symptoms after treatment;
- coexistence of menstrual and gastrointestinal manifestations within different Mizaj profiles;
- Mizaj-specific patterns of PMOS-related clinical manifestations; and
- clinical and biochemical safety during treatment.

Safety Monitoring

Clinical tolerability was evaluated throughout the intervention period. Participants were questioned regarding any adverse symptoms arising during treatment. CBC, liver function and renal function results available before and after treatment were reviewed to identify possible hematological, hepatic or renal safety signals.

Any adverse events occurring during the follow-up period were to be documented in the clinical record irrespective of their presumed relationship to the Unani intervention.

Statistical Analysis

Considering the exploratory nature of the study and the small sample size of 20 participants, statistical analysis was primarily descriptive. Categorical variables, including Mizaj category, gastrointestinal symptoms, menstrual abnormalities and clinical response, were summarized as frequencies and percentages.

Continuous variables, where available, were to be summarized using mean with standard deviation for approximately normally distributed data or median with interquartile range for non-normally distributed data.

Gut-related symptoms were evaluated individually according to their presence or absence at baseline and follow-up. Symptom frequencies were tabulated for the overall cohort and separately for the four Mizaj categories. Menstrual patterns were similarly evaluated at baseline and after the three-month intervention.

Data analysis was performed using statistical software and version 26.0, with all analyses based on available clinical observations.

RESULTS

A total of 20 women aged 18–40 years with previously documented PCOS/PMOS were included in this preliminary clinical case series. Participants were equally distributed across the four predefined Mizaj categories: Damvi, Balghami, Safravi, and Saudawi, with five participants in each group. Thus, each Mizaj category represented 25.0% of the total study population.

Although all participants shared a clinical diagnosis of PMOS, considerable heterogeneity was observed in their presenting constitutional, metabolic, gastrointestinal, and menstrual manifestations. Weight gain or central adiposity was more

prominent among women with Damvi and Balghami Mizaj, while hyperandrogenic manifestations such as acne and hirsutism were particularly evident in the Safravi profile. Participants with Saudawi Mizaj commonly demonstrated menstrual irregularity, fatigue, and difficulty in reducing weight.

Table 1. Distribution of participants according to Mizaj profile

Mizaj profile	Number of participants (n)	Percentage (%)
Damvi	5	25.0
Balghami	5	25.0
Safravi	5	25.0
Saudawi	5	25.0
Total	20	100.0

The equal representation of the four Mizaj categories facilitated descriptive evaluation of differences in clinical symptom patterns but should not be interpreted as reflecting the natural prevalence of these temperaments among women with PMOS.

Distinct patterns of PMOS-associated manifestations were observed across the four Mizaj categories. Damvi participants predominantly demonstrated central obesity or weight gain, facial acne, increased appetite, a sensation of heaviness, and menstrual irregularity. Balghami participants were characterized primarily by weight gain, central adiposity, lethargy, reduced physical activity, and menstrual disturbance.

Among Safravi participants, acne, excessive hair growth or hirsutism, irritability, heat intolerance, and weight-related or metabolic complaints constituted the major presenting features. The Saudawi group commonly exhibited difficulty with weight reduction, fatigue, menstrual irregularity and, where documented, hyperpigmentation and altered appetite-related symptoms.

Table 2. Predominant PMOS-related clinical manifestations across Mizaj profiles

Mizaj profile	Predominant PMOS-related manifestations
Damvi	Central obesity/weight gain, facial acne, increased appetite, heaviness, menstrual irregularity
Balghami	Weight gain, central obesity, lethargy, reduced physical activity, menstrual irregularity
Safravi	Acne, hirsutism/excessive hair growth, irritability, heat intolerance, weight/metabolic complaints (altered bowel habit)
Saudawi	Difficulty in weight reduction, fatigue, menstrual irregularity, possible hyperpigmentation and appetite-related complaints (loss of appetite)

These observations demonstrate clinical heterogeneity among women diagnosed with the same endocrine-metabolic condition and formed the basis for exploring gastrointestinal manifestations in relation to constitutional Mizaj.

Gastrointestinal complaints were documented across all four Mizaj categories, although the predominant patterns differed between constitutional groups.

Women with Damvi Mizaj predominantly reported abdominal bloating and fullness, with occasional constipation. The Balghami group showed a pattern suggestive of relatively sluggish gastrointestinal function, characterized by constipation, bloating, flatulence, and sluggish digestion.

Among women with Safravi Mizaj, bloating was accompanied by altered bowel habits and dyspeptic symptoms. In comparison, Saudawi participants predominantly experienced constipation, abdominal discomfort, bloating, and flatulence.

Thus, bloating represented a recurrent gastrointestinal complaint across multiple Mizaj profiles, whereas constipation appeared particularly prominent in the Balghami and Saudawi profiles. Dyspeptic and altered bowel symptoms were comparatively more characteristic of the Safravi pattern.

Table 3. Predominant gut-related symptom patterns according to Mizaj

Gut-related symptom	Damvi	Balghami	Safravi	Saudawi
Bloating	Predominant	Predominant	Predominant	Predominant
Constipation	Occasional	Predominant	Not identified as predominant	Predominant
Abdominal fullness/discomfort	Predominant fullness	—	—	Predominant discomfort
Flatulence	—	Predominant	—	Predominant
Sluggish digestion	—	Predominant	—	—
Dyspeptic symptoms	—	—	Predominant	—
Altered bowel habit	—	—	Predominant	—

The findings suggest that different Mizaj profiles may exhibit distinguishable gastrointestinal symptom clusters. However, because individual-level symptom counts were not available, no statistical comparison of gastrointestinal symptom prevalence between Mizaj groups was performed.

Menstrual disturbance was a consistent feature across the study population, although the nature of the abnormality varied among the four Mizaj categories.

Damvi participants predominantly demonstrated irregular or delayed menstruation with prolonged menstrual cycles. Women with Balghami Mizaj commonly presented with delayed, scanty, or irregular menstruation. Irregular and delayed menstrual cycles were also the principal abnormalities documented in the Safravi group.

Among Saudawi women, menstrual abnormalities appeared to include irregular, delayed, or scanty menstruation. Dark or blackish menstrual flow was additionally documented within the clinical description of this group.

Table 4. Predominant menstrual patterns across different Mizaj profiles

Mizaj profile	Predominant menstrual pattern
Damvi	Irregular/delayed menstruation; prolonged menstrual cycle
Balghami	Delayed, scanty, and irregular menstruation
Safravi	Irregular/delayed menstruation
Saudawi	Irregular, delayed or scanty menstruation; dark/blackish menstrual flow where documented

Menstrual irregularity therefore represented a common clinical manifestation across all Mizaj profiles, while differences were observed in cycle delay, menstrual quantity, and associated characteristics.

The descriptive evaluation demonstrated coexistence of gastrointestinal and menstrual complaints within each Mizaj profile. In the Damvi group, irregular or delayed menstrual cycles occurred in association with bloating and abdominal fullness. Balghami participants showed delayed or scanty menstrual patterns together with constipation, bloating, flatulence, and sluggish digestion.

Safravi participants displayed irregular or delayed cycles alongside bloating, altered bowel habits, and dyspeptic complaints. In the Saudawi profile, irregular and scanty menstrual patterns occurred in association with constipation, abdominal discomfort, bloating, and flatulence.

Table 5. Coexisting gastrointestinal and menstrual manifestations according to Mizaj

Mizaj	Predominant gastrointestinal pattern	Predominant menstrual pattern	Overall clinical pattern
Damvi	Bloating, abdominal fullness, occasional constipation	Irregular/delayed menstruation, prolonged cycle	Abdominal fullness/bloating accompanying menstrual irregularity
Balghami	Constipation, bloating, sluggish digestion, flatulence	Delayed/scanty and irregular menstruation	Sluggish bowel function accompanying delayed/scanty menstruation
Safravi	Bloating, dyspeptic symptoms, altered bowel habit	Irregular/delayed menstruation	Dyspeptic/altered bowel symptoms accompanying menstrual irregularity
Saudawi	Constipation, abdominal discomfort, bloating, flatulence	Irregular/delayed/scanty menstruation	Constipation-dominant GI pattern accompanying menstrual disturbance

These observations indicate possible Mizaj-specific clustering of gut and menstrual manifestations. Given the small number of patients within each group, the patterns should be interpreted as preliminary clinical observations rather than evidence of a statistically established association.

Participants received individualized therapeutic regimens according to their assessed Mizaj and clinical presentation. The Damvi group received Regimen 1, consisting primarily of Majoon Dabeed-ul-Ward, Habbe Tinkar, and Sharbat Bazoori Motadil. Balghami participants received Regimen 3 comprising Jawarish Zanjabeel, Arq Mako, and Arq Kasni.

The Safravi group was managed with Regimen 2, which included Habbe Rasaut, Itrifal Ustukhuddus, and Arq Brinjasaf. Saudawi participants received Regimen 4 consisting of Itrifal Gududi together with a Joshanda containing Nankhwah, Badiyan, and Waj Turki administered in relation to the expected menstrual cycle. Each Regimen participant received Habbe Mudīr at a dose of two tablets twice daily (BD) for 5 consecutive days, initiated immediately prior to the expected onset of menstruation, after which the medication was discontinued.

All participants additionally received lifestyle advice consisting of approximately 30 minutes of walking daily and restriction of junk food, fatty foods, and fried foods.

DISCUSSION

The present preliminary clinical case series explored gut-related symptom patterns among women with Polyendocrine Metabolic Ovarian Syndrome (PMOS) classified according to four Unani Mizaj profiles. The principal observation was

that gastrointestinal complaints were present across all four constitutional groups, but the predominant pattern differed according to Mizaj. Bloating was observed as a recurring clinical feature across the profiles, whereas constipation and symptoms suggestive of relatively sluggish bowel function were more characteristic of the Balghami and Saudawi groups. Damvi participants predominantly showed bloating and abdominal fullness, while Safravi participants demonstrated a comparatively different gastrointestinal pattern characterized by bloating, dyspeptic symptoms, and altered bowel habits. Menstrual irregularity was common across all four profiles, although delayed, scanty, or prolonged menstrual patterns differed between groups. These findings support the clinical heterogeneity of PMOS and suggest that gastrointestinal symptoms may constitute an under-recognized component of its broader symptom burden.

The occurrence of gastrointestinal complaints in the present series is consistent with emerging evidence linking PCOS, the historical diagnostic terminology underlying PMOS, with functional gastrointestinal disturbances. Wei et al., in a systematic review and meta-analysis, reported significantly greater odds of irritable bowel syndrome (IBS) among women with PCOS than among controls, with a pooled odds ratio of 2.23 [11]. Importantly, IBS commonly incorporates symptom domains such as abdominal discomfort, bloating, constipation, diarrhea, or changes in bowel habits; however, the gastrointestinal manifestations documented in the present study should not be equated with a diagnosis of IBS because standardized Rome criteria were not applied. A recent review by Saei Ghare Naz et al. similarly concluded that a possible relationship exists between PCOS and IBS, although the mechanisms remain incompletely defined and could involve metabolic abnormalities, hormonal variation, neurotransmitter regulation, psychological factors, and lifestyle influences [12]. Thus, the recurrent bloating, constipation, abdominal discomfort, and altered bowel habits observed in the present case series are clinically plausible within the wider gastrointestinal symptom spectrum reported among women with PCOS/PMOS, but they require confirmation using validated gastrointestinal diagnostic instruments.

A particularly interesting observation was the presence of bloating across all four Mizaj profiles. Rather than indicating a Mizaj-specific manifestation, this finding may suggest that bloating represents a relatively nonspecific gastrointestinal complaint accompanying PMOS in susceptible individuals. Increasing evidence has implicated alterations in the gut microbial ecosystem in PCOS. Li et al. conducted a systematic review and meta-analysis involving 28 studies with 1,022 women with PCOS and 928 controls and reported reductions in several measures of gut microbial diversity, together with alterations in bacterial taxa associated with short-chain fatty-acid production and bile-acid metabolism [13]. Similarly, Sola-Leyva et al. found significantly reduced gut microbial alpha diversity among women with PCOS in a systematic review and meta-analysis, although they emphasized substantial methodological heterogeneity related to ethnicity, body mass index, study design, and microbiome assessment methods [14]. These studies provide biological support for further investigation of the gut in PMOS but do not establish that clinically reported bloating in the present patients resulted from microbial dysbiosis.

The constipation-dominant pattern observed among the Balghami and Saudawi participants deserves particular consideration. Balghami women in the present series showed constipation, bloating, sluggish digestion, and flatulence together with weight gain, central obesity, lethargy, and reduced physical activity. Saudawi participants similarly demonstrated constipation, abdominal discomfort, bloating, and flatulence, although their accompanying constitutional and menstrual characteristics differed. These observations cannot establish that Mizaj determines intestinal motility. Nevertheless, they suggest that future studies could examine whether differences in dietary intake, physical activity, adiposity, insulin resistance, autonomic function, and bowel transit contribute to the apparent clustering of gastrointestinal symptoms within these constitutional profiles.

This consideration is particularly relevant because metabolic phenotype itself may influence the gut environment in PMOS. Zhang et al. described a close and potentially bidirectional relationship among obesity, insulin resistance, hyperandrogenism, PCOS, and gut microbiota alterations [15]. Obesity may aggravate the metabolic expression of PCOS through insulin resistance and hyperandrogenemia, while dietary and metabolic factors can simultaneously influence intestinal microbial composition. In the current series, weight gain and central obesity were particularly evident within the Damvi and Balghami clinical profiles. Consequently, gastrointestinal differences observed between Mizaj categories could partly reflect differences in body composition, dietary patterns, metabolic status, or physical activity rather than Mizaj alone. Because body mass index, waist circumference, insulin resistance indices, dietary intake, and stool microbiome characteristics were not systematically quantified in this preliminary study, these potential confounding pathways could not be examined.

Furthermore, intestinal microbial abnormalities are not restricted to women with obesity. Mammadova et al. evaluated lean women with PCOS and demonstrated differences in the abundance of several intestinal microbial taxa compared with BMI-matched healthy women, although overall bacterial richness and diversity did not differ significantly between groups [16]. Their findings are important in interpreting the current results because they indicate that gut-related biological alterations in PCOS cannot be explained solely by obesity. Hyperandrogenism and endocrine phenotype may also contribute. Therefore, the variation in gastrointestinal presentation across Mizaj categories in the present study could conceivably reflect an interaction among constitutional features, metabolic characteristics, hormonal disturbances, dietary exposures, and gastrointestinal physiology rather than any single underlying mechanism.

The Safravi pattern was distinguishable from the more constipation-predominant Balghami and Saudawi presentations. Safravi participants showed acne, hirsutism, irritability and heat intolerance together with bloating, dyspeptic symptoms, and altered bowel habits. This observation is of interest because emerging microbiome research has suggested an

association between androgen excess and intestinal microbial variation in PCOS. However, the present study did not measure serum androgen concentrations in relation to gastrointestinal symptoms and therefore cannot determine whether the hyperandrogenic clinical features observed among Safravi women were biologically related to their gastrointestinal presentation. The finding should instead be regarded as a clinically observed symptom cluster that warrants targeted investigation.

Recent meta-analytic and genetic evidence further illustrates the complexity of the gut–PCOS relationship. Min et al. combined a meta-analysis with bidirectional Mendelian randomization and identified associations between particular microbial genera and PCOS susceptibility [17]. Although such studies strengthen the rationale for investigating gut-related mechanisms, microbiome findings remain heterogeneous across populations, and the clinical meaning of individual bacterial differences has not yet been sufficiently established for routine patient stratification. Accordingly, it would be inappropriate to infer from the present symptom-based case series that any individual Mizaj corresponds to a particular microbial signature. Future studies integrating Mizaj assessment with stool microbiome sequencing, metabolomics, inflammatory markers, fasting insulin, glucose, and androgen profiles would be required before such relationships could be evaluated objectively.

Menstrual irregularity was another consistent finding across all four Mizaj profiles. Damvi participants predominantly showed irregular or delayed menstruation and prolonged cycles; Balghami women displayed delayed, scanty, and irregular menstruation; Safravi women showed irregular or delayed cycles; and Saudawi participants demonstrated irregular, delayed, or scanty menstruation. The presence of menstrual dysfunction across every constitutional category is consistent with the central reproductive expression of PMOS and reinforces the observation that Mizaj groups in this study represented variations within the same underlying syndrome rather than discrete diseases. Of particular interest was the coexistence of menstrual and gastrointestinal manifestations within each profile. This coexistence may justify future studies examining whether changes in gastrointestinal symptoms parallel changes in menstrual regularity, metabolic status, or hormonal parameters.

The Mizaj-based characterization used in this study also offers an individualized clinical perspective. Yilmaz recently reviewed the concept of Mizaj in women's health and described Damvi, Safravi, Balghami, and Saudawi as constitutional profiles reflecting combinations of hot/cold and wet/dry characteristics, emphasizing that temperament-based assessment is historically intended to recognize inter-individual variation in clinical presentation and management [18]. The findings of the present study are compatible with this individualized framework in the limited sense that women carrying the same PMOS diagnosis exhibited different clusters of constitutional, gastrointestinal, and menstrual manifestations. However, Mizaj remains a traditional constitutional construct and should not be interpreted as equivalent to contemporary biological classifications based on insulin resistance, androgen concentration, body mass index, inflammatory phenotype, or microbiome composition.

There is limited published clinical literature specifically evaluating Mizaj in women with PCOS. Qayoom investigated temperament-related characteristics among women with PCOS within an Unani clinical setting and highlighted the relevance of constitutional assessment in understanding the heterogeneous clinical presentation of the syndrome [19]. The current case series extends this line of inquiry by focusing specifically on gastrointestinal symptom patterns rather than restricting observation to reproductive or metabolic characteristics. Nevertheless, direct comparison between the two studies should be undertaken cautiously because of differences in study design, sample size, clinical assessment, and outcome definition.

All participants in the present series received individualized Unani management selected according to Mizaj and clinical presentation, together with lifestyle advice incorporating regular walking and restriction of junk, fatty, and fried foods. Because each Mizaj group received a different therapeutic regimen, the present design cannot determine whether any subsequent clinical change was attributable to the pharmacological formulations, lifestyle modification, natural variation in symptoms, regression to the mean, or other factors. Lifestyle intervention itself may modify important components of PCOS. A systematic review and meta-analysis by Khatlani et al. reported that lifestyle interventions in overweight and obese women with PCOS can improve body weight and selected markers of insulin resistance and cardiometabolic risk [20]. Thus, lifestyle advice represents a clinically relevant component of management, but it also prevents attribution of any observed post-treatment response solely to the prescribed Unani formulations.

The available safety observations are reassuring but preliminary. Baseline and post-intervention CBC, liver function tests, and renal function tests were reported to remain within normal limits during the three-month clinical follow-up. Nevertheless, the small sample size and limited observation period are insufficient to establish the safety profile of the individualized regimens. Larger studies should incorporate systematic adverse-event surveillance, standardized biochemical monitoring, treatment adherence assessment, and clearly defined criteria for treatment discontinuation.

Several limitations should be considered when interpreting these findings. First, the study included only 20 women, with five participants in each Mizaj category, and was therefore not powered to determine statistically significant differences among constitutional groups. Second, the equal representation of the four Mizaj profiles was a feature of the assembled case series and cannot be interpreted as the natural distribution of Mizaj among women with PMOS. Third, there was no non-PMOS control group and no untreated or comparator intervention group. Fourth, gastrointestinal manifestations were documented clinically without a validated symptom instrument or formal diagnostic criteria for functional gastrointestinal

disorders. Fifth, objective measures of intestinal physiology, stool microbiota, microbial metabolites, inflammatory markers, dietary intake, insulin resistance, and androgen status were unavailable. Sixth, different Unani regimens were used in different Mizaj groups, making between-group comparison of therapeutic response inappropriate. Finally, the currently available dataset does not contain complete numerical individual-level pre- and post-treatment symptom severity scores; consequently, treatment effect sizes, response percentages, statistical significance, and causal treatment claims cannot be reliably generated.

Despite these limitations, the study has value as a hypothesis-generating clinical series. It directs attention toward gastrointestinal manifestations that may otherwise receive limited consideration during conventional PMOS assessment and examines them within an individualized Unani constitutional framework. The apparent clustering of abdominal fullness in Damvi women, constipation and sluggish digestion in Balghami women, dyspeptic and altered-bowel symptoms in Safravi women, and constipation with abdominal discomfort in Saudawi women provides a clinically testable hypothesis for future research. Prospective studies should recruit substantially larger samples, apply a validated Mizaj assessment instrument, standardize gastrointestinal symptom measurement, quantify menstrual patterns objectively, and include anthropometric, metabolic, hormonal, inflammatory, and microbiome parameters. Such studies could determine whether the symptom clusters observed here are reproducible and whether Mizaj provides information beyond established metabolic and reproductive phenotyping.

CONCLUSION

This preliminary case series suggests that gut-related symptoms are common within the clinical spectrum of PMOS and may show differing patterns across Mizaj profiles. Bloating was a recurring manifestation across all groups, whereas constipation-dominant symptoms were more characteristic of Balghami and Saudawi profiles, dyspeptic and altered bowel symptoms were prominent in Safravi participants, and abdominal fullness was notable among Damvi participants. Menstrual irregularity coexisted with gastrointestinal complaints across all four profiles. These observations do not establish a causal relationship between Mizaj and gastrointestinal dysfunction, nor do they demonstrate a microbiome mechanism or comparative therapeutic efficacy. Rather, they provide a preliminary clinical framework for larger prospective studies integrating Unani constitutional assessment with standardized gastrointestinal, endocrine, metabolic, and microbiome evaluation.

ACKNOWLEDGMENT

The authors sincerely acknowledge the In-charge, RRIUM Mumbai, for facilitating the necessary institutional support and facilities required for conducting this case study.

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