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Dr. Kouser Fathima Firdose
Lecturers, Dept. of Ilmul Qabalat wa Amraze Niswan, National Institute of Unani Medicine, Bangalore, Karnataka, India

Dr. Ismath Shameem
Lecturers, Dept. of Ilmul Qabalat wa Amraze Niswan, National Institute of Unani Medicine, Bangalore, Karnataka, India

Correspondence
Dr. Ismath Shameem
Lecturers, Dept. of Ilmul Qabalat wa Amraze Niswan, National Institute of Unani Medicine, Bangalore, Karnataka, India

An approach to the management of poly cystic ovarian disease in Unani system of medicine: A review

Dr. Kouser Fathima Firdose and Dr. Ismath Shameem

Abstract
Polycystic ovarian disease (PCOD) is the most common endocrine abnormality of women of reproductive age, and is the commonest cause of infertility due to anovulation. PCOD affects 5-10% of reproductive age women rising till 15% in women with infertility. This disease has been described by eminent *Unani* Physicians in the classical literary books under the headings of amenorrhoea, obesity, phlegmatic disease and liver disorders.In this review we outline clinical features, presentation and pathogenesis of polycystic ovarian disease (PCOD), treatment objectives and therapeutic options in Unani perspective. We focus on and outline the role of the Unani system of medicine in diagnosis and treatment of this condition. We also review recent information of herbal drugs having effect on insulin resistance in PCOD. Finally, we outline the current and future mode of treatment for this common condition in women. Unani concept of PCOD is mainly based on the dominance of *khilte balgham* (phlegm). The predominant symptoms of PCOD like amenorrhoea, oligomenorrhoea and obesity have been attributed to arise of phlegm. So it is claimed that PCOD arises due to predominance of phlegm in the body which leads to cyst formation in the ovaries, obesity and amenorrhoea. This disease is complex, as it further gives rise to complications like infertility, cardiovascular ailments, type-2 diabetes mellitus, metabolic syndrome, carcinoma of breast and endometrium. Such a complicated disease has no satisfactory treatment till now and most often patient gets only symptomatic treatment with hormones and insulin sensitizer and becomes drug dependent in the long term. Unani physicians have recommended regular induction of menstruation as one of treatment modality applied for women who has developed masculine features suggestive of PCOD. They have given a line of management based on correction of temperament, menstrual regulation by use of emmenagogue drugs and local application of herbs to reduce the severity of hair growth, acne and hyper pigmentation due to PCOD.

Keywords: PCOD, Menstrual irregularities, Unani medicine, Insulin sensitizers, herbal drugs.

Introduction

The modern civilization has given rise to various life style diseases. The sedentary life style, craving towards the junk food, emotional and behavioral disturbances (like highly competitive attitude and social insecurities); all these factors disturb the HPO Axis (hypo thalamus- pituitary-ovarian axis) and perpetuate life style diseases like PCOD [1]. This disease is considered as the commonest endocrine abnormality in women of reproductive age affecting 5-10% of the reproductive women rising till 15% in women with infertility [2] and it accounts for about 75% of anovulatory infertility. It results in production of high amounts of androgen particularly testosterone and chronic anovulation. Hyperandrogenism manifest clinically as hirsuitism, acne, alopecia and virilization [3]. PCOD accounts for most cases of oligomenorrhoea and about a third of those of amenorrhoea. History, examination, and first line investigations usually establish the diagnosis [4]. A more recent joint consensus statement between the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) has revised the criteria for diagnosis of PCOD to include two from three of the following criteria: i) oligomenorrhoea/anovulation; ii) clinical or biochemical evidence of hyperandrogenism; iii) polycystic ovaries, with the exclusion of other etiologies. The hallmark clinical features of PCOD are menstrual irregularities (amenorrhoea, oligomenorrhoea, or other signs of irregular uterine bleeding), signs of androgen excess, and obesity [5]. This disease is complex and it further gives rise to serious complications like infertility, cardiovascular ailments, type-2 diabetes mellitus and carcinoma of breast and endometrium [1]. The onset of this disease is peri–menarcheal, as during this stage major endocrinological and emotional change takes place and this probably could explain the reason behind its onset at this stage [6].

Methods
Authentic ancient text of Unani medicine was searched to obtain the Unani concept of PCOD. PubMed/Google scholar was also searched with the keywords; Herbs for PCOD, Insulin sensitizers, phytohormones etc.

Unani concept
The Unani term coined for PCOD is *Marz Akyas Khusytur Rehm*; is in fact an Arabic translation of PCOD. This disease has been described by *Unani* Physicians under the headings of amenorrhoea, obesity, phlegmatic disease and liver disorders [7-9]. Unani concept of PCOD is mainly based on the dominance of *khilte balgham* (phlegm). It has been mentioned in classical books that *sue mizaj barid* (abnormal cold temperament) of the liver may leads to abnormal production of phlegm, [10] as liver is unable to convert chyme into blood, instead it converts it into phlegmatic blood or tenacious phlegm. One of the abnormal forms of phlegm is *balgham mayi,* which is thinner in consistency and can accumulate in sacs to form cysts [11]. Also the other predominant symptoms of PCOD like amenorrhoea, oligomenorrhoea and obesity have been attributed to rise of phlegm [7, 9] Hence, it is claimed that PCOD arises due to predominance of phlegm in the body which leads to cyst formation in ovaries, obesity and amenorrhoea. The Unani Physicians consider that the early twenty years of life are the period of childhood which is predominated by phlegm; hence the phlegmatic disorders are more likely to occur at this stage. This probably may explain the role of phlegm as a contributing factor for the onset of this disease during this age group [7, 9, 10].

Diagnosis by clinical presentation
Rhazes recorded combination of signs conjoined with menstrual irregularities (oligomenorrhoea, amenorrhoea and DUB) including hirsutism, obesity, acne, hoarseness of voice and infertility, which are suggestive of polycystic ovarian disease and hyperandrogenism [8]. Hippocrates (460-370 BC) first documented the affiliation of excess facial and body hair (hirsutism) in females with prolonged amenorrhoea, obesity and infertility; [7] similar observations were reported by Galen (130-200 AD). Hirsutism is mentioned in classical Unani literature as a complication of prolonged amenorrhoea associated with other masculine features like hoarseness of voice, male body contour, acne etc. [7, 9] The pathophysiology of hirsutism was explained by *Ibn Sina* and *Ismail Jurjani.* Alteration of normal temperament of women was considered as central dogma for hirsutism. It was said that persistence of amenorrhoea for a long duration causes alterations in internal environment of women's body and status of equilibrium is disturbed, leading to formation of some unwanted material which is being excreted through skin pores in the form of *busoore labnia* (acne) and also participate in the growth of thick hair over the body [7, 9, 10]. As the normal temperament of women are cold and moist and with prolonged amenorrhoea, it gets transformed towards that of men (hot and dry). This is mainly because of the *ehteraq* (detonation) of normal phlegm (cold and moist) to black bile (hot and dry) [8]. The effect of this *souda* (black bile) on skin leads to hirsutism and hyper pigmentation (acanthosis nigricans) [4].

It was observed by *Ibn Sina, Ismail Jurjani* and *Al Razi* that development of masculine features is more common in obese women with robust body and prominent blood vessels, as these women have almost similar temperament as that of men [7-9]. PCOD may complicate further leading to infertility, insulin resistance, metabolic syndrome etc [12]. Such a complicated disease has no satisfactory treatment till now and most often patient gets only symptomatic treatment with hormones and insulin sensitizers but becomes drug dependent in long term.

Management
Current and Potential Treatments: [2]

Women with PCOD are currently treated according to their presenting features like irregular periods, infertility and hirsutism.

- Oral contraceptives in menstrual disturbance.
- Clomiphene citrate, ovarian drilling/ laser treatment and assisted reproductive techniques in anovulatory infertility.
- Cyproterone acetate, ethinylestradiol and spironolactone in hirsutism and acne.
- Weight loss in menstrual disturbance and anovulatory infertility helps in improvement of metabolic perturbances and reduces the risk of coronary heart disease.
- Insulin sensitizing agents (such as metformin) in obesity, androgen excess, menstrual disturbance, anovulatory infertility and metabolic perturbances.

In Unani system of medicine, treatment is based on four categories

1. *Ilaj bil Tadbeer* (Regimenal therapy): [10, 11]

- Lifestyle modifications including regular exercise, brisk walk, diet control and adequate sleep.
- If the patient is obese, weight reduction is advised; this can be facilitated by *hammame yabis* (steam bath) and *dalak* (massage).
- To induce menstruation, *hijama* (wet cupping) is applied over the calf muscles of both lower limbs to divert the flow of blood towards the uterus.

2. *Ilaj bil Ghiza* (Dietotherapy): [7, 8, 11, 13]

- Diet should be light, nutritious and easily digestible.
- Use of fibrous food including green leafy vegetables and fresh fruits.
- Avoid cold and dry food, late digestible food, heavy and spicy food.
- Drink plenty of fluids.

3. *Ilaj bid dawa* (Pharmacotherapy): [7-9,13]

Rhazes recommended regular induction of menstruation as one of treatment modality applied for women who has developed masculine features suggestive of PCOD**.** He has given a line of management based on correction of temperament and menstrual irregularity by use of emmenagogue drugs (single or compound) and local application of herbs to reduce severity of hair growth, acne and hyper pigmentation.

4. *Ilaj bil Yad* (Surgical Treatment) [7, 9]

Fasd (venesection) of *Rage Safin* (saphenous vein) to divert the flow of blood towards the uterus to induce menstruation.

***Usoole Ilaj* (Principles of Treatment)** [8-10, 13]

- *Idrar haiz* with use of *mudire haiz* drugs.
- *Tadeel mizaj* with use of *munzij wa mushil balgham* drugs
- Weight reduction
- Specific drugs

***Mudire Haiz* (Emmenogogue) Drugs:** [10]

a) Single Drugs: *Abhal, Badiyan, Post Amaltas,, Persiawa Shan, Asgand, Aspand, Habbe Balsan, Habbe Qillt, Habbe Qurtum, Rewand Chini, Tukhme Kasoos, Khashkhash, Gule Teesu, Karafs, Elwa, Heeng, Jausheeer, Asaroon, Turmus, Tukhme Gazar.*

b) Compound formulations: *Habbe mudir, Joshanda mudir haiz, Sharbat buzoori, Murakkabate foulad* etc [8, 9, 13].
These emmenagogue drugs are used with uterine tonics like *majoon muqawwi rehm* which consists of *asgand* only as it contains phytohormones which induces the menstruation by maintaining hormonal balance.

2. *Tadeel Mizaj* (Correction of temperament): [8-10, 13]
a) *Munzij: Mavez Munaqqa, Badiyan, Aslusoos, Persia wa Shan, Anjeer Zard*
b) *Mushil: Ayarij Faiqrah, Turbud, Habun Neel* with *Arqe Badiyan.*
c) *Tabreed: Khameera Gauzaban Sada* wrapped in *Warqe Nuqra*

3. Weight Reduction: [8, 9]
a) *Dawae Luk Sagheer* with *Arqe Badiyan*
b) *Safoofe Muhazzil* with *Arqe Zeera.*
c) *Itrefil Sagheer* at bed time.

4. Specific Drugs:
a) Use of insulin sensitizers like *Darchini, Rewand, Abhal, Mushktramashi, Zafran, Asgand* etc. [4, 14]
b) Natural drugs for hirsutism like *Nagarmotha, Amba Haldi, Methi, Pudina, Soy*a, *Neem, Kalonji* etc. [13, 15]

Despite of many herbs named, experimental studies have been conducted on few to explore pharmacological activities of these herbs and are associated with diverse limitations.

Abhal/Juniper* (*Juniperus communis*)-*Figure 1 and ***Mushktramashi/ Pennyroyal* (*Mentha pulegium*) -*Figure 2***: They can be used in cases of PCOD, as clinical study on oligomenorrhoea, the retrospective finding was that 12 out of 19 cases of PCOD in the pretrial scan were reported to be normal in the post-trial USG of pelvis, along with restoration of menstruation. Hence, this formulation regulates menstruation through its effect on the ovaries [14].

Fig 1: *Juniper*

Fig 2: *Pennyroyal*

Neem* (*Azadirachta indica*)-*Figure 3 and ***Zanjabeel (Zingiber officinalis)-Figure 4* :** They can be used in PCOD, as clinical study conducted on PCOD showed that 20 patients had PCOD at base line and after treatment, it persist in 6 patients only. This effect is attributed to anti-androgenic, hypoglycemic and insulin sensitizing activities of these drugs which serves as an alternate option in PCOD. [15]

Fig 3: *Neem*

Fig 4: *Zanjabeel*

***Satavar* (*Asparagus recemosus* Wild) -*Figure 5*:** It can be used in PCOD, as clinical study conducted on infertility showed that11 patients had PCOD before treatment, while on post treatment scan; only 1patient had same findings. This effect is attributed to the presence of phytoestrogens- steroidal saponins in this drug which exert hormone like action in the body.[16]

Fig 5: *Satavar*- plant & root

***Aslussus*/Liquorice (*Glycyrrhiza glabra*) -*Figure 6*:** Clinical studies conducted on liquorice confirmed that it reduces serum testosterone probably due to the block of 17-hydroxysteroid dehydrogenase and 17-20 lyase in PCOD. [17]

Fig 6: *Liquorice*

***Pudina*/Spearmint (*Menthaspicata* Labiatae)–*Figure 7*:** RCTs carried out on patients of hirsutism with spearmint tea, confirmed that it has anti-androgenic properties as free and total testosterone levels and degree of hirsutism were reduced. Hence, it could be a natural alternative for women having mild hirsuitism. [18]

Fig 7: *Spearmint*

Darchini*/Cinnamon ((*Cinnamomum zeylanicum*)–*Figure 8: Clinical trial on PCOD women showed significant reduction in insulin resistance by increasing phosphatidylinositol 3-kinase activity in the insulin signaling pathway due to the presence of insulin potentiating factor which enhances the insulin activity in carbohydrate metabolism. [17]

Fig 8: *Cinnamon*

***Alsi* /Flaxseed (*Linum Usitatissimum*) - *Figure 9*:** Clinical trial conducted on PCOD patients using flaxseed (30 gm/day) showed significant decrease in serum insulin, serum total and free testosterone levels. [19]

Fig 9: *Flaxseed*

***Elwa* /Aloe vera (*Aloe barbadensis*) – *Figure 10*:** Animal trial on female rats using aloe vera gel confirmed that it exerts a protective effect against PCOD by restoring the ovarian steroid status and altering steroidogenic activity due to the presence of phyto-components.

Fig 10: *Aloe vera*

***Methi/* Fenugreek (*Trigonella foenum-graecum*)- *Figure 11*:** It is used in PCOD patients with diabetes and

hyperlipidemia, as it improves glucose tolerance & lowers the cholesterol level. [17]

Fig 11: *Fenugreek*

Khar khask/ Puncture Vine (Tribulus terrestris) –Figure 12**:** It is an effective female fertility tonic, ovarian stimulant & act as an excellent choice for women with PCOD. [19]

Fig 12: *Puncture Vine*

***Kalonji* (*Nigella sativa* Linn) – *Figure 13*:** *Kalonji* oil was proved to be effective in patients of insulin resistance syndrome and in alleviating the obesity mainly due to its insulin sensitizing action. Various components of *kalonji* like thymoquinone, thymol, unsaturated fatty acids, lipase and tannins are responsible for its beneficial effects in insulin resistance syndrome. [20, 21]

Fig 13: *Kalonji seeds*

In order to prove significant safety and efficacy of herbs, further well-designed randomized clinical trial with double blinding, on large sample size should be conducted.

Conclusion

PCOD is a common disease that has received intensive study over the last 50 years; we still know remarkably little about its complex etiology. We have, however, learned much about the consequences and diagnosis of this disease. The recent diagnostic criteria outlined in the EHSHRE/ARM consensus statement is a move in the right, the same can be well correlated with the descriptions given by renowned Unani Physicians in their respective treatises. Positive women's reproductive health care is the ultimate goal of all gynecologists. In this regard, alternate therapeutic protocols have been followed to improve the quality of life. Potential treatment options in Unani medicines includes *Idrar haiz, Tadeel mizaj,* Weight reduction, Specific drugs like insulin sensitizers can be used to alleviate the ailing eves from this complicating disease.

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