An Overview of Polycystic Ovarian Disease Associated Secondary Amenorrhoea in Unani System of Medicine

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Abstract: Polycystic ovarian syndrome (PCOS) is a heterogeneous disorder, with multiple reproductive, cosmetic and metabolic complexities which is characterized by dysfunction in ovulation and clinical or biochemical hyperandrogenism and the presence of polycystic ovarian morphology. Women with PCOS have increased rate of insulin resistance and hyperandrogenism which have been implicated in the dysfunction of HPO-Axis, leading to anovulation and menstrual irregularities. In classical Unani text, it is mentioned that ihtibas-i-tams usually occurs in women with balghami mizaj and fair complexion, and is mainly caused by dominance of khilti-balgham, which increases the viscosity of khun-i-hayd and form sudda, as a result menstrual blood fails to expelled out of the uterus. The treatment available in conventional medicine is oral use of hormone therapy and insulin sensitizing agents, but this treatment has got its own side effects and complications. Several medicines are available in Unani system of medicine, which act as insulin sensitizer, uterotonics and causes withdrawal bleeding in patients with PCOS associated amenorrhoea. This review article gives a detailed description of PCOS associated secondary amenorrhoea including its etiopathogenesis, diagnosis, principle of treatment in Unani system of medicine.

Keywords: PCOS, Secondary amenorrhoea, Herbal insulin sensitizer, Unani system of medicine.

1. Introduction

PCOS is the most common gynecological endocrinopathy of child bearing aged women characterize by hyperandrogenism, ovarian dysfunction, and polycystic ovarian morphology, which affects approximately 4 to 12% of whole female population. Secondary amenorrhoea occurs in 10-20% of patients complaining of infertility and is one of the commonest reasons for referral to a gynecological endocrine clinic.² It has been estimated that secondary amenorrhoea, has a prevalence ranging from 3 to 4% in reproductive age group women.³⁻⁴ Adams et al. (1986), found PCOS in 26–30% of patients with amenorrhoea, and in 87% with oligomenorrhoea.⁵ The prognosis depends on the cause of amenorrhoea. Secondary amenorrhoea associated with PCOD will respond to treatment.⁶ The available treatment in conventional medicine is hormone therapy (for withdrawal bleeding and menstrual regulation) and also use of insulin sensitizing agents (to reduce insulin resistance and androgen levels as well as to improve ovulatory function) in women with PCOS.⁷ Metformin, the most widely used drug in PCOS is often poorly tolerated because of gastrointestinal side effects.⁸⁻¹² and hormonal therapy though effective in menstrual cyclicity, has got its own complications like venous thrombo-embolism, stroke, breast, endometrial and ovarian cancer and are contraindicated in patients with hypertension, cardiac diseases, liver diseases, DVT etc.⁶ Conventional pharmaceutical management is limited by the prevalence of contraindications in women with PCOS, non-effectiveness in some circumstances, side effects and by preferences of women with PCOS for alternatives to pharmaceutical management.¹⁴ Hence, there is an increase demand for herbal therapy which is to be safe, effective and easily available. The treatment plan in Unani system of medicine for secondary amenorrhoea in PCOD patients is based on the concept that, treat the cause of amenorrhoea i.e. PCOD with life style modification through tadbir, ghiza and dawa.¹⁵⁻¹⁶ use of qawi mudirr-i-hayd advia¹⁷ to induce menstruation,¹⁸ use of munzij wa mushil-i-balgham advia for tanqia-i-badán¹⁸⁻¹⁹ and finally use of Unani medicines which act as insulin sensitizers in PCOD patients.²⁰

2. Material & methods

For Unani concept of disease, available authentic text of Unani Medicine was searched. Literature was also searched on PubMed, Google Scholar, Medline, Science Direct with the keywords; PCOS, secondary amenorrhoea, herbal insulin sensitizer, Unani system of medicine etc.

Unani Concept: Unani physicians mentioned the description of PCOD under the headings of amenorrhoea, obesity, phlegmatic diseases and liver disorders.¹⁵⁻¹⁸

Ihtibas-i-tams (Amenorrhoea): In classical Unani text, it is defined as cessation of menstruation,¹⁹⁻²¹ as either it varies from scanty flow to complete cessation or it occurs at interval of ≥2 months. Duration of inter menstrual period ranges from 20 to 60 days and if it exceeds, above this level then, it is considered as abnormal and called as ihtibas-i-tams.²² It usually occurs in women having balghami mizaj and fair complexion¹⁵ and such women generally suffer from ussr-i-tams,¹⁶⁻²² as heavy menstrual bleeding may occur after a long period of amenorrhoea.¹⁹

Etiopathogenesis:
General symptoms: Headache, dyspnoea and chest pain on exertion, palpitation, fainting, indigestion, loss of appetite, nausea, excessive thirst, constipation, heaviness in the body, restlessness, dysuria, low urine output, high coloured urine, excessive sleep, salivation, tiredness, obesity etc.

Specific symptoms: Ghalba-i-balgham: Patient is obese, puffy and flabby body, cold skin, pale face, prominent vessels, nabz- bati and mutafawit, bawl- sufaid, ghaliz and kasir, baraz-balghami, menstrual blood is red in colour and thin in consistency, and scanty pubic hair.

Figure 1: Ashabe Ihtibas-i-tams specific to PCOD

a) Su’-i-mizaj barid causes sudda formation in uterine blood vessels due to excessive intake of fluids, which in turn leads to amenorrhea and infertility.

b) Akhlat-ighaliz mainly balgham increases the viscosity of blood due to lazujat. This ghaliz madda gets accumulates in the blood after intake of ghaliz and sakhit ghiza and forms sudda, which blocks the uterine vessels and results in amenorrhea.

c) Zo’afi-jigar causes amenorrhea via three factors:

- Blood flow to distant organs fails as liver is unable to convert chyme into blood, instead it converts it into blood after intake of unani balgham.
- Improper tawild-i-khuin (defective haemopoiesis).
- Formation of sudda within the liver, which results in obstruction in blood flow towards the uterus.

d) Faribihi causes amenorrhea in three ways:

- Excessive fat deposition on the uterus compresses the uterine blood vessels.
- Sudda formation due to excessive accumulation of balgham in uterine vessels.
- Alteration in the ovarian function due to dominance of rutubat and burada in the body, which causes tul ihtibas-i-manai (chronic anovulation) which results in menstrual irregularities and infertility.

Diagnosis: It is based on clinical presentation of the patient-

Complications: Ibn Sina states that when blood goes towards the uterus (which is a natural passage for excretion of menstrual blood) and if it does not find the way to escape out from the body; it will return back to the body, and when this process is repeated several times, it results in complications such as:

- ikhtinaq al-rahim (hysteria), sayalan al-rahim (leucorrhoea), waram al-sulb sawdawi wa saqirus rafig (uterine tumours and malignancy), uqr (infertility), waram al-jigar (hepatitis), istisqa (ascitis), awram-i-ahsha (visceral inflammation), malankholia, generalised anasarca etc.

Ibn Sina states that amenorrhea is associated with tul ihtibas-i-manai, faribihi, and uqr and such type of women resembles men. Thus, a well established association exists between anovulation, amenorrhea, obesity, and infertility which correlate with polycystic ovarian disease.

Hirsutism: It is mentioned as a complication of prolonged amenorrhea associated with other masculine features like hoarseness of voice, male body contour, acne etc.

Ibn Sina and Ismail Jurjani explained the basic pathophysiology of hirsutism as variation in normal temperament of women. If amenorrhea persists for a long duration, it causes alterations in internal environment of the body and disturbed the equilibrium status of women, leading to growth of excessive hair over the body. The normal temperament of women gets transformed towards that of men due to prolonged amenorrhea, which is mainly due to ihtiraq of balgham to sawada which leads to hirsutism, hyper pigmentation (acanthosis nigricans) and formation of some

Zo’afi-i-jigar: Patient present with h/o liver diseases and c/o heaviness in right hypochondium, whitish coloured urine seldom mixed with blood and change in skin colour. On examination- hardness felt in right hypochondric region.

Sudda: Menses stops gradually, feeling of heaviness in the body, abdominal distension due to flatulence, and change in skin colour.

Sometimes amenorrhea results in marked changes in the body structure such as, appearance of excessive hair growth on the body mainly on face, hoarseness of voice, and change in temperament of the organs as well as the body. These changes mainly occur in those women who are multiparous; having muscule features, prominent vessels and such women resembles men (Jalinoos).
unwanted material which is being excreted through skin pores in the form of busur-i-labaniyyah (acne).\textsuperscript{15} 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.\textsuperscript{17,18}

**Acne Vulgaris (Busur-i-labaniyyah):** These are small white eruptions on the face, which resemble condensed drop of milk, thus named as muhasa (Ibn Sina).\textsuperscript{23} These eruptions are caused by maddu-i-sadidiya (infected matter) which comes towards skin surface due to buharat-i-badan.\textsuperscript{19,26} Generally, it appears in young girls between 16-25 years of age due to menstrual disturbances or amenorrhoea.\textsuperscript{19}

**Usul-i-ilaj:**

1. **Life style modification:**
   **Ilaj bi’l ghiza:**
   - *Taqlil-i-ghiza*\textsuperscript{15,17}
   - Use mulattif aghzia like\textsuperscript{15,23} lukewarm water or sirkalkanj in empty stomach.\textsuperscript{30}

   **Diet allowed:**
   - Use qalil al-tagghiya wa kasir al-kamiya’t ghiza\textsuperscript{17,31} like vegetables & fruits which fills the stomach.\textsuperscript{16,26}
   - Add spices such as filfil, raai, zeera, lehsan to the vegetables;\textsuperscript{18} use plain soup, vegetables with dry chapatti.\textsuperscript{15}

   **Diet restricted:**
   - Avoid cold water,\textsuperscript{17,18} milk, butter, mutton, fish,\textsuperscript{32} oily and fried food.\textsuperscript{33}

   **Ilaj bil-tadbir:**
   - *Riyazat:* Riyazat-i-qawi\textsuperscript{15,17,23} to reduce body weight.\textsuperscript{18}
   - *Dalak:* Natun or zijf balut followed by hamnam can reduce fat accumulation.\textsuperscript{15}
   - *Abzan:* Joshanda of mulattif drugs such as shibbat, marzanjosh, pudina, sadab, babuna, aqeequl malik, sa’atar, qardmana, kalonji, heeng, asaaron, tagar, doqor.\textsuperscript{18,23}
   - *Takmid:* Takmid at lower abdomen with har advia mainly advia-i-muhammira as it stimulates blood flow towards the uterus.\textsuperscript{15,18}

   - *Zimad:* Joshanda of har and mulattif advia\textsuperscript{18,23} over lower abdomen.\textsuperscript{18}
   - *Huqna:* Sheham hanzal, ro’ghan zaitoon, namak, bortiq.\textsuperscript{5,23}
   - *Humul:* Shehad, ro’ghan sosan, mur, samagh kankaz, asal musaffa, sakbeenaj, muqil, ro’ghan sosan, and mur.
   - *Firzaja:* Ma’al-asal, ro’ghan sosan and murmakki.\textsuperscript{15}
   - *Hamnam-i-yabes:* It is recommended in obese women before taking meals,\textsuperscript{31} and after the procedure, advice her to sleep for some time, then use small quantity of food.\textsuperscript{34}
   - *Fasd:* Fasd of rag-i-safin\textsuperscript{17} and rag-i-mabiz as it diverts the flow of blood towards the uterus to induce menstruation.\textsuperscript{15,23}
   - *Hijama:* Application of hijama over the calf muscles is more beneficial in comparison to fasd of rag-i-safin to induce menstruation, in obese and robust women having narrow uterine vessels and whose blood is thin; as venesection fails to evacuate the sufficient amount of blood from the narrow uterine vessels but the cupping does, as it purifies the blood.\textsuperscript{15,35} Hijama at sa’aq forcefully absorb morbid matter from the upper part of the body\textsuperscript{19} and divert it towards the uterus.\textsuperscript{23} It is applied 2 or 3 days prior to the expected menstruation, one day on one calf followed by its application on next day on second calf to induce menstruation.\textsuperscript{15,17,18} Hijama works on the principle of tanqia-i-mawad and

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**Figure 2:** Principles of treatment in Unani medicine

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removes the toxic blood from the body, thus it detoxify the body.\textsuperscript{35}

**Ilaj bi’l dawa:**
- Use \textit{ma’al-usal} with mulattif and \textit{har mulidlik} like joshand \textit{post-i-khyarshamer}, mushtaramashi, parsiyaushan, qand siyah kohna etc.\textsuperscript{23}
- \textit{Mudirat-i-harra} advia like parsiyaushan, badian, khubazi, zooja, tukhm sudab, ansoo, biranjasif, gust sheerin, hab balsan, kalonji, ajmood, pudina, ajwain etc\textsuperscript{26}
- Use \textit{ma’j}un having demulcent property e.g: tiraq-i-kabeer, ma’jun-i-kamooni,\textsuperscript{19} ma’jun-i-biladuri.\textsuperscript{30}

**2-Use of gawi mudirr-i-hayd advia:**

**Oral use:**
- Ayarij and loghazia,\textsuperscript{16} afawiya, fiwowah.\textsuperscript{15}
- Joshanda turmus and surkh lobiya with shehad or joshanda turmus with mur and sudab.
- Mushtatatamashi, abhal, majeeth each 1 part, tukhm-i-karafs, soanf, elaichi khurd, behroza, sakbeenaj, jausheer, mastagi, each 1/2 part; all ingredients are finely powdered and used in a dose of 5 g with joshanda turmus and lobiya surkh after adding shehad.
- Sikanjabeen-i-usuli with habb-ul-ghar 4 g and behroza 2 g.\textsuperscript{19}
- Prepare tablet of muqil, mur, abhal in equal quantity and used in a dose of 10.5 g.\textsuperscript{23}
- Prepare tablet from the extract of majeeth, mushtaratamashi, kardmana, sudab, abhal and heeng, each 2 g and used in a dose of 35 g.\textsuperscript{15}
- **Single Drugs:** Darchini, ayarij feeqra, sakbeenaj, jausheer, junbedastar, kardmana, tukhm marzanjosh, mushtaratamashi, abhal, majeeth, pudina nehr, pudina kohi, afsanteen, soanf, kibir, karafs, ansoo, sudab, zaraawand, irsa, bakhar maryam, ashanan, asaroon, izkhar, gust, habb-ul-ghar, javitri, o’od balsan, ushq, marmakki, indrain, farfiyoon, kalonji, turmus, lobiya etc.\textsuperscript{15,17,19,23}
- **Compound formulations:** Qurs abhal, ma’jun abhal, sharbat bazari, sharbat kasooos, sharbat ja ada, sharbat biranjasif, sharbat saleekha, naq zujur, \textsuperscript{17,23} dhamarsa, ayarij feeqra, loghazia, aqras mur, sharbat afsanteen.\textsuperscript{19}

**Local use:**

**Humul:**
- Farfiyu\textsuperscript{15} or farfiyu\textsuperscript{18,30} or bikh-i-badam talkh, usara brinjasif with mur, zaraawand, ro’ghan aqehwan.\textsuperscript{17}
- Ashnan farsi, aaqarqarha, kalonji, sudab taza, farfiyuin in equal quantity, mixed with ganda behroza and used with ro’ghan zanbaq.\textsuperscript{15,17}
- Muqil 35 g, jausheer, asal labni, harf, kardmana, tukhm jandeer, jundbedaster and ro’ghan sosan.

**Dhuni:**
- Nankhwah\textsuperscript{15} hamal, jausheer, kardmana, hileet, sakbeenaj\textsuperscript{15} tukhm karafs, heeng,\textsuperscript{18} Karam kalla or behroza, jausheer, gandhak daughed in zehra gau.\textsuperscript{19}
- Methi,\textsuperscript{15} jundbedaster, nakhkhitki, izfarutteeb, o’od, miy’a saila.

**Abzan:**
- Sudab, abhal, karafs, karnab, raziyana,\textsuperscript{16} mushtaramashi.\textsuperscript{17}
- Tukhm karafs, karnab, raziyana, sudab, biranjasif, abhal, footnaj.\textsuperscript{16}

**Zimad**
Apply paste of biranjasif over suprapubic region\textsuperscript{15} or tukhm bedanjeer over umbilical region.\textsuperscript{21}

**Takmid: Mudir and aromatic drugs**
- Afawiya (over umbilical and suprapubic region).\textsuperscript{15,17,23}
- Prepare joshanda with coarse powder of balcharh, darchini, javitri, jaiphal, elaichi gust, aqqaia over the umbilical region.\textsuperscript{19}
- Sambul, saleekha, darchini, o’od balsan, hab balsan, javitri, jausheer, elaichi khurd wa kalan, gust, hamama, shaguya izkhar.\textsuperscript{13,16}

**Huqna:**
- Ro’ghan yasmeen with ro’ghan nardeen,\textsuperscript{16} or ro’ghan sumbul or gust or chambli.
- Abhal, turmus, lobiya surkh each 35 g, majeeth, afsanteen, pudina, balcharh, sudab khussh, izkhar each 7 g. shoneez, kundas, behroza, jausheer each 4 gm, boil in water and mix ro’ghan yasmeen. Use 100 ml decoction after adding jundbedaster 1 g and sprinkle za’fran over it.\textsuperscript{19}

**3-Use of munzij wa mushil-i-balgham advia:**\textsuperscript{15,32}

**Oral:**
- Tanjia-i-balgham with hab ayarij or hab sakbeenaj and expel out ghalliz madda via qa’i,\textsuperscript{18,23} if balgham-i-lauz j fails to get evacuated, same can be expelled out via ishal.\textsuperscript{17}
- Ma’al-usul with ro’ghan bedanjeer 7 g, ayarij feeqrah 1.047 g and use every morning for 7-9 days.\textsuperscript{18}
- Ma’al-usul, ro’ghan arand with hab muntin.\textsuperscript{18}
- Joshanda afiimoon\textsuperscript{25} or post-i-khayarshamer, parsiyaushan, qand siyah kohna.\textsuperscript{23}
- Powder of mastagi, zanjabeel, zeera siyah, each 1 g with jawarish jalinoos 7 g.
- Joshanda pudina khussh, elaichi khurd wa kalan, each 5 g; zanjabeel, zeera siyah, ansoo each 3 g, mixed with khameera banafscha 50 g and used in the morning. Sheera prepared from badian 5 g, zeera siyah, zanjabeel, ansoon 3 g, arg elaichi 120 g, with khameera banafscha 4 g and used in evening.\textsuperscript{24}
- Mashruditus, sanjareena, dawa’al-misk har, tiraq-i-faroog, ma’jun filasifa, and other har ma’jun and jawarishat.\textsuperscript{25}

**Local:**

**Zimad:** Karnab and methi,\textsuperscript{18} tukhm bedanjeer,\textsuperscript{23}

**Huqna:** Joshanda babuna, soya, marzanjosh, methi, anjeer khussh mixed with ro’ghan kunjud.

**Humul:**
- Ro’ghan bedanjeer or ro’ghan nardeen or gazardashiti.\textsuperscript{18}
- Za’fran, sumbulutteeb, shib yamani, o’od, sazij hindi, anzarut, charbi murghabi and zard-i-baize murgh.
- Jausbua, kazmazj, phitkari biryan, post amar each 4.5 g finely powdered.\textsuperscript{23}
Acne vulgaris:
- Joshanda methi, marzanjosh, babuna, soya.\(^{18}\)
- Joshanda shibbat, pudina, marzanjosh, sudab, babuna, akkeleel malik, sa’ar.\(^{21}\)

Dhuni:
- Zaraneekh surkh, mur, jauzsr, miy’a, qinna, habbal-ghar; used after menses.
- Muqil, ushq, ilakulambat, shoneez.\(^{15}\)

Use of munzij wa mushil-i-sawda advia for hirsutism & acne vulgaris:
**Usul-i-Haj:** Oral use of tanqia-i-badan with munzij-mushil therapy followed by topical application of mujaffif and muhallil advia for acne & haliq and mukhaddir advia for hirsutism.\(^{19,29}\)

Hirsutism:
- First apply, lime with lead carbonate\(^{26}\) for removal of hair, followed by application of nagarmotha, amba haldi, methi, pudina, soya, neem, kalonji to prevent further hair growth.\(^{20}\)
- Tukhm utangan with ro’ghan or asagopol with sirka or jundbedaster with shehad.\(^{19}\)

Acne vulgaris:
- **Nuskha Matbukh:** Post halela zard 7 g, post halela kabli 17 g, aftimoon 20 g, ustukhuddus and gul-i-banafsha each 14 g, bisfajj fastuqi 10.5 g, first boil haleqat and bisfajj in 3 litre of water till 750 ml water remains, afterwards add ustukhuddus and gul-i-banafsha and boil till 500 ml water remains, then add aftimoon after rapping in a cloth and boil for 2 or 3 times and put off the fire, allow it to cool down by itself and filtrate it.
- Elwa 3.5 g, gharigoon, maghz bil each 2 g, namak hindi 1.75 g, kharbaq siyah 860 mg, all ingredients are ground to make fine powder, then doughed in sugar syrup and used followed intake of nuskha matbukh 2 to 3 hours later.

Local use:
- **Tila-i-Musasa:** Irsa, post-i-saroos, barg shibbat, aard-i-jau, safaida kashagiri, all in equal quantity ground in goat’s milk.\(^{28}\)
- Shoneez, naushadar and bura armani mixed with sirka.\(^{28}\)
- Murdar sang, bura armini, with ro’ghan gul or kalonji with sirka.
- Gil-i-armani, bura ushman sabz and tukhm kharbuza.\(^{19}\)

4- Use of Unani medicines which act as insulin sensitizers:
- Mechanism of action of herbal insulin sensitizers: These medicinal plants act on insulin sensitivity via various cellular and metabolic targets and the principle sites of target are the liver, adipocytes and muscles. These potential plants targeted insulin action via several pathways: inhibition of hepatic glucose production or potentiating the peripheral glucose utilization in the muscles and adipocytes by regulating the activity and expression of key enzymes and glucose transporters. In addition, a lot of medicinal plants improve insulin sensitivity through the stimulation of insulin-signaling pathways. Herbal insulin sensitizers are methi,\(^{37,38}\) karela,\(^{39}\) jamun,\(^{40}\) haldi,\(^{41}\) zaitoon,\(^{42}\) darchini,\(^{43,44}\) kalonji,\(^{45}\) zanjabeel,\(^{46,4}\) gurmar,\(^{48}\) saffran,\(^{49}\) elwa,\(^{50}\) etc.

3. Conclusion
Polycystic ovary syndrome (PCOS) is a complex, reproductive and endocrine disorder affecting up to 17.8% of reproductive aged women characterized by polycystic ovaries, chronic anovulation and hyperandrogenism leading to symptoms of oligo/amenorrhea, hirsutism, acne, and infertility. Conventional pharmaceutical management is limited due to contraindications in women with PCOS, non-effectiveness in some circumstances, side effects and by preferences of women for alternative management. In USM effective treatment is available with fewer side effects and recurrence rate; but experimental studies were conducted on few Unani medicines, that too on small number of patients with variations in dosage & duration of treatment. Hence, future trials are recommended on large sample size for longer duration to prove the efficacy and safety of Unani drugs in the management of secondary amenorrhea in PCOD patients.

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