



## A Comprehensive Review on Polycystic Ovarian Syndrome (PCOS) and its Management in Unani System of Medicine

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### ABSTRACT

Virtually every woman will suffer a gynaecological condition at some point in her life. It can be devastating or minor as well. Polycystic ovarian syndrome [PCOS] is to be most common endocrine disorder found in women of reproductive age. Women with PCOS may have infrequent or prolonged menstrual periods or excess male hormone [androgen] levels, weight gain, acne, difficulties in pregnancy. The ovaries may develop numerous small collections of fluid [follicles] and fail to regularly release eggs. The latest estimation of W.H.O indicates polycystic ovarian disease has affected 116 million women [3.4%] worldwide. Treatment of PCOS is primarily targeted to correct the biochemical abnormalities. Weight reduction in obese person is the first line of treatment 2-5% reduction in weight improves the metabolic syndrome and reproductive function. Exercise is found beneficial. Unani physicians described the PCOS under the headings of qillate tams, ehthebase tams, and uqr.uqr [infertility] is an advanced stage. Jalinoos says women become amenorrhoeic if her mizaj transformed towards masculinity and develops the features like male pattern hair growth, hoarseness of voice etc. Curative measures are elimination of existing causes [Correction of Metabolism]/Islahe Jigar, Correction of Sue Mizaj Barid, following Asbabe Sitta Zarooriyah, Ilaj Bit Tadbeer.

### 1. INTRODUCTION

Polycystic ovarian syndrome (PCOS) was first described in 1935 by American gynaecologists Stein and Leventhal as a syndrome manifested by amenorrhoea, hirsutism and obesity associated with enlarged polycystic ovaries (Dutta-2016). It is also called as hyper androgenic anovulation (Kollmann *et al.*, 2014) or Stein-Leventhal syndrome (Islam *et al.*, 2014). It is the one of the most common causes of oligo-ovulatory infertility and it is the most common endocrinopathy affecting premenopausal women (Franks, S.-1995; Goudas and Dumesic-1997). The prevalence of PCOS varies from 2.2% to 26% in different countries and has been reported as 7.1% based on national institute of health (NIH) criteria (Richard Scott Lucidi-2011) and has 14.6% based on Rotterdam criteria (Aziz *et al.*, 2015). It starts appearing at 15 to 25 ages and it may take years for

its clinical presentation to appear (Peri and Levine-2007). The World Health Organization estimates that it effects 116 million people among 15 to 49 year old woman worldwide as of 2010 (Islam *et al.*, 2016). In this condition, more than 12 follicles are produced every month but as they all are immature. So no ovum is releases and resultantly, ovaries start producing higher level of testosterone, which leads to hormonal imbalance. One fourth population of women are having multiple follicles in ovary, but only 10% women suffer from PCOS. It is characterized by oligomenorrhoea, obesity, hyperandrogenism and infertility (Shaikh Nikhat-2016). The condition appears to have a genetic component (Govind *et al.*, 1999; Calvo *et al.*, 2001; Jahanfar *et al.*, 1995; Hague *et al.*, 1998) and those effected often have been both male and female relatives with adult onset diabetes, obesity, elevated blood triglyceride, high blood pressure and female relative with infertility, hirsutism, and menstrual problem (Kahsar *et al.*, 2001). PCOS is associated with increased pregnancy loss and other complications of pregnancy such as gestational diabetes mellitus (Lanzone *et al.*, 1995). Women with PCOS also have an increased risk of endometrial carcinoma. Although PCOS is known to be associate with reproductive morbidity, diagnosis is especially important because PCOS is now thought to increase metabolic and cardiovascular risks such as myocardial infarction, atherosclerosis, coronary artery

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disease by Nestler, J. E. (1999). In unani system of medicine, the disease has not been described under the term of PCOS. But *warm e raham*, *warm e aana*, and *warm e khusiyat ur rahem* (Ovary) are diseases present in unani literature with same picture of PCOS. PCOS can be present in any *mizaj* and any *khilth*. For example, PCOS can be present in patient with *su e mizaj e safra, sauda* and also *balgham*<sup>[17]</sup>. According to Hippocrates the main cause of disease is impairment of humours (*Akhlat*). *Uqr* (Infertility) is an advanced stage in majority cases of PCOS. Mainly *Sue mizaj barid* causes *uqr* by *toole ehtebase mani* (Chronic anovulation) by Dr. Mastaan. Symptoms like obesity and hirsutism associated with amenorrhoea or oligomenorrhoea are clearly described in classical texts. Further *Jalinoose* says women become amenorrhic if her *mizaj* transformed towards masculinity and develops the features like male pattern hair growth, hoarseness of voice etc., (IbnSina-2010). In conventional medicine treatment of PCOS is adopted according to a specific cause; goals of therapy include ameliorating hyper androgenic symptoms by use of anti-androgen drugs, including ovulation, regulating menstruation and preventing cardio-metabolic complications (Shamiss et al., 1992). All these therapies are being used for treating PCOS but they have their own limitations. Most of these drugs are costly, having potential side effects and producing only symptomatic relief. Most of the drugs used for the induction of ovulation are having serious manifestations like Ovarian Hyper Stimulation Syndrome, multiple pregnancies, ascites and thromboembolism by Nestle, J. (1998).

## Etiology

This heterogenous disorder is characterized by excessive androgen production by the ovaries mainly. PCOS is a multifactorial and polygenic condition.

Dysregulation of CYP 11a gene, upregulation of enzymes in androgen biosynthetic pathway have been suggested. Insulin receptor gene on chromosome 19p13.2 are also involved.

**Diagnosis** is based upon the presence of any two of the following three criteria [American society of reproductive medicine (ASRM)/ European society of human reproduction and embryology (ESHRE), 2003].

1. Oligo and/or anovulation.
2. Hyperandrogenism (clinical and/or biochemical)
3. Polycystic ovaries.

Other etiologies [congenital adrenal hyperplasia (CAH)], thyroid dysfunction, hyperprolactinemia, Cushing syndrome are to be excluded. Also this dysfunction is results of life long interaction of environment (Pollution), lifestyle (Sedentary life) and chronic inflammation. Other contributing factors are Obesity (about 50% of women are obese), stress and excessive intake of junk food (D.C.Dutta-2016). Based on the Unani concept, impairment of humours (*Akhlat*), *sue mizaj barid* of *rehm* [which causes increase in the viscosity of (*Khilthe balgham*)], *Zoofe jigar*, *sudda* (Obstruction) are the major causes (Shaikh Nikhat-2016).

## Sign And Symptoms

Common symptoms of PCOS include the following:

### 1. Menstrual disorders:

PCOS mostly produces oligomenorrhoea (few menstrual periods) or amenorrhoea (no menstrual periods), but other types of menstrual disorders also occur (Teede et al., 2012; Gnana Priya, R-2015).

### 2. Infertility:

This generally results directly from chronic anovulation (lack of ovulation).

### 3. High levels of masculinizing hormones:

The most common signs are acne and hirsutism (male pattern of hair growth), but it may produce hypermenorrhoea (heavy and prolonged menstrual periods), androgenic alopecia (increase hair thinning or diffuse hair loss), or other symptoms. Approximately three quarters of people with PCOS (by the diagnostic criteria of NIH/NICHD 1990) have evidence of hyperandrogenemia.

### 4. Metabolic syndrome:

This appears as a tendency towards central obesity and other symptoms associated with insulin resistance. Serum insulin, insulin resistance and homocysteine levels are higher in women with PCOS (Nafiyeh et al., 2010).

## Management

Management of PCOS needs individualization of the patient. It depends on her presenting symptoms. Like menstrual disorder, infertility, obesity, and hirsutism or combined symptoms. Patient counselling is important. Treatment is primarily targeted to correct the biochemical abnormalities.

### 1. Weight reduction

Weight reduction in obese patients is the first line of treatment. Body mass index (BMI) <25 improves menstrual disorders, infertility, impaired glucose intolerance (insulin resistance), hyperandrogenemia (hirsutism, acne), and obesity. Weight reduction (2-5%) improves the metabolic syndrome and reproductive function.

### 2. Exercise

Being physically active is very important in managing PCOS. It has been shown to improve symptoms and reduce the risk of developing related long term health conditions. For women with PCOS there are many benefits of regular exercise, including:

- a) Peripheral muscle cells metabolize 80% of glucose.
- b) Improved self-confidence and motivation.
- c) Reduced anxiety and depression.
- d) Improved menstrual regularity and fertility.
- e) Help with weight maintenance or weight loss.

Aerobic exercise (3-4x/wk 20-30 min/session) burns 100-200 kcal and there is 40% improvement in insulin sensitivity

within 49 hrs.

Research has shown any type of regular exercise is effective in improving PCOS symptoms. Whether it is moderate or vigorous aerobic exercise or resistance (using weights) exercise, women's PCOS symptoms will improve (Paola, S. 2016).

### 1. Diets

Diet recommended for obese PCOS patients are low in calories with a reduced carbohydrate intake, and any form of these diets can produce the 5%-10% loss necessary to re-establish ovarian functions in these patients. In 2005 Reaven suggested that low fat diets produce a decrease in hyperinsulinemia, which improves metabolic effects.

### 2. Surgery

Laparoscopic ovarian drilling (LOD) is done for cases found resistant to medical therapy. Ovarian surface cysts are punctured upto a depth of 2-4 mm. The cysts are vaporized using monopolar cutting current (20-30W). 5-8 punctures are made in each surgery. It has replaced the conventional wedge resection of the ovaries. Pregnancy rates following ovarian diathermy are higher. Bariatric surgery may be indicated in some PCOS women who are morbidly obese.

### 3. Ovulation induction

In PCOS, anovulation relates to low FSH concentrations and the arrest of the antral follicle growth in the final stages of maturation. Excess LH, androgens, and insulin may individually or collectively play a direct or indirect role in this process, augmenting steroidogenesis but arresting follicular growth. For many women, anovulatory infertility is the presenting complaint. Medications and other options available for the induction of ovulation are reviewed in the following sections.

### 4. Clomiphene Citrate

CC constitutes one of the first line treatments for ovulation induction in these patients, as it is economical, is straight forward, has few adverse effects, and requires little monitoring. Clomiphene triggers the brain's pituitary gland to secrete an increased amount of follicle stimulating hormone (FSH) and LH (lutinizing hormone). This action stimulates the growth of ovarian follicle and thus initiates ovulation. During normal menstrual cycle only one egg is ovulated. The use clomiphene often causes the ovaries to produce two or three eggs per cycle. CC is indicated in patients with PCOS and anovulation with normal FSH levels, it has certain limitations in patients with a BMI > 30 and advanced age.

Doses of 50-150 mg are administered for 5 days, starting on days 3 or 5 of a progestin-induced or spontaneous cycle. CC produces ovulation in 75-80% of PCOS patients, although when the gestation rate is assessed, it nears 22% per ovulation cycle. These differences in results are attributed to the antiestrogenic effects of CC, mainly on the endometrium and the cervical mucus. The live birth rate following 6 months of clomiphene ranged from 20% to

40%. Furthermore, the majority of pregnancies occur red within the first six ovulatory cycles following the initiation of treatment.

### 5. Metformin

Metformin improves metabolic syndrome by reducing all the parameters: weight, BMI (hyperinsulinemia, hyperandrogenism), BP and lipid abnormalities. 500 mg thrice daily s found to correct the biochemical abnormalities. After 1 week, the dose is increased to 1000mg for another week and then to 1500mg daily. Clinical response is usually seen at the dose of 1000 mg daily. It appears that some PCOS patients who do not respond to metformin at a dose of 1500 mg daily will respond favourably to 2000 mg daily. Pioglitazone and rosiglitazone are also being used in cases, resistant to metformin.

### 6. Glucocorticoids

Glucocorticoids such as prednisone and dexamethasone have been used to induce ovulation. In PCOS patients with high adrenal androgen, low-dose dexamethasone (0.25-0.5 mg) at bedtime can be used. In a study of 230 women with PCOS who failed to ovulate with 220 mg of CC for 5 days, addition of 2 mg of dexamethasone from days 5-14 is associated with a higher ovulation rate and cumulative pregnancy rate. Enthusiasm for their use is dampened, however, by their potential adverse effects on insulin sensitivity; therefore, prolonged use should be discouraged.

### 7. Gonadotropin

The mechanism of action of gonadotropins is to induce ovulation, maintain and provoke optimum follicle growth via the controlled administration of FSH, and achieve a follicle capable of being fertilized. The main drawback of gonadotropins is that they provoke multiple developments, thereby increasing the risk of ovarian hyper stimulation syndrome (OHSS) and multiple pregnancies.

Several treatment protocols have been advocated, such as step-up, low dose step-up, and step down regimens. A step-up dose finding approach favouring unifollicular development is recommended. The step-up regimen starts with a minimum dose (37.5-50 IU/day), which increases according to lack of follicle response. The step-down regimen starts with the maximum recommended dose, which is reduced as a follicular response is achieved.

### 8. In vitro fertilization techniques

These techniques are used as a last resort when treatments with CC, gonadotropins and letrozole have failed. IVF is the first choice in cases of concomitant diseases both in women (severe endometriosis, tubal obstruction, etc.) and man (azospermia, male factor) that reduce effectiveness of other techniques. Because of the increased risk of multiple gestations (up to 10%) with gonadotropin induction in anovulatory women with PCOS, IVF is a reasonable alternative for women seeking pregnancy. IVF with a single embryo transfer significantly reduced the risk of multiple gestations.

## Treatment

Treatment for PCOS usually starts with lifestyle changes like weight loss, diet, and exercise. Losing just 5 to 10 percent of body weight can regulate the menstrual cycle and improve PCOS symptoms. Weight loss also improves cholesterol levels, lower insulin, and reduces heart disease and diabetes risks.

### Treatment of menstrual dysfunction

Endometrial biopsy is done in patients with PCOS who have not had menstrual bleeding for a year or longer. Some investigators have advocated the use of ultrasonography to determine thickness in deciding whether to do a biopsy of the endometrium. Endometrial proliferation can be inhibited by administering either cyclic progesterin or oral contraceptives with a combination of estrogen and progesterin (Badawy and Elnashar, A-2011).

### Unani Treatment

In Unani concept there is no description of disease with this name. But *warm e raham*, *warm e aana*, and *warm e khusiyat ur rahem* (ovary) are the diseases present with same picture of PCOS. PCOS can be present in any *Mizaj* and any *Khilth*. For example PCOS can be present in patient with *su e mizaj e safra*, *sauda* and also *balgham*. The treatment methodology of the Unani system of medicine is called *ilaj bil Zid*<sup>[28]</sup>. It means, the medicine which has the opposite *Mizaj* of the affected *akhlat* is chosen and the patient treated with it. *Usul e ilaaj* (line of treatment) include *tanqiya e mawad*, *idrar e haiz*, *muhallilat e auram*, *muhallilat e sulaat* (anti-tumour), *ilaaj bil giza*, *ilaaj bit tadbeer*.

### PCOS with *sue mizaj safra*

Diagnose PCOS with *khilt e galib*, if *safra* cyst will be due to *sozish*.

Other symptoms of *safra*- like palpitation, restlessness, giddiness, hyperacidity, severe premenstrual pains are also may present or not.

### Useful unani medicines for *safra*

*Kishneez*, *Saunf*, *Hari Ilaichi*, *Podina*, *Gulab*, *Haldi*, *Lahesan*, *Kalonji*, *Makoh Kasni*, *Naag Kesar*, *Kapur*, *Kachri*.

Apply oil made with *kalonji* and *lahesan* on lower abdomen. Oil of *Nirgundi* or *Sambhalu* is also useful.

Murakkab are *jawarish zaroori sada*, *khamira gaozaban sada*

### PCOS with *sue mizaj balgham*:

Dull look, dull pain, *nabz*, and other *balghami* symptoms are present.

### Useful unani medicines for *balgham*

For *Ghir tabayee Balgham*, give following Unani *joshanda* (Decoction) which have the action of *Munzija e Balgham* in a

dose of half a cup morning and the evening for 12 to 14 days.

### **Munzija e Balgham**

*Badiyan*, *Asal e soos*, *Usthukhudoos*, *Izkhar*, *Perciaushan*, *Zeer e Siya*.

After maturation / coctives of *Ghair e tabayee Mada*, the maturation *mada* has to be expelled by giving *Mushilath* (Purgatives). If the involved *mada* is *Ghair Tabayee Balgham* give *Joshanda* for 3 days.

### **Mushil e Balgham**

*Sheham e Hanzal*, *Bisfaij*, *Turbud*, *Sibr*, *Sena makki*, *Amalthas*. *Murakkab* are *itrifal ustukhudus*, *itrifal zamani*, *majun anjeer*.

### PCOS with *sue mizaj sauda*

Typical picture of metabolic syndrome with *pcos* are present with *sauda* like *dandruff*, *central obesity*, *hard cysts*, *Tasallub e sharain*, *Tasallub e nabz*.

### Useful unani medicines for *sauda*

*Methi*, *Zeera*, *Kaba Chini*, *Filfil Siyah*, *Pipli*, *Babuna*, *Nakhuna*, *Suddab*

Apply oil made with *Zeera*, *Methi*, and *Suddab*,

### **Munzija e sauda**

*Badranj boya*, *Usthukhudoos*, *Baiyan*, *Thuranjabeen*, *Shahathira*

It is prescribed in the dose of half a cup morning and the evening for 12 to 14 days.

But, if the *Ghir Tabayee Sauda* is *Ghaleez* in *Khiwam* then we should give the *munzija* in recurrently. In this condition selection of *dawa* should also have the action of *Mudir-e-Haiz* (Emmenagogue) and *Muqawwi e A'za e Rayeesa* (General tonic for vital organs) by Gani.

### **Mushil e Sauda**

Give *joshanda* of following drugs for 3 days *Haleel e Siya*, *Jamal gota*, *Sheham e Hanzal*, *Aftmoon*, *Sena makki*.

*Murakkab* are : *Itrifal Usukhudus* – Dissolves cyst and also have *Idrar e Haiz* activity.

*Sharbat e Deenar* \_ Anti-inflammatory activity.

*Al Hayateen* has also same function as *Sharbat e Deenar*.

### Some useful medicines

*Tukhm e Hayat* or *Beej Paneer* – Five seeds soak in one cup of water at night. In morning use *khaisanda* only.

It increases the insulin sensitivity and reduces obesity which is beneficial in PCOS.



It has anti inflammatory activity.

All antidiabetes is useful in PCOS like, Karela, Jamun, Methi, Gudmar.

All anti inflammatory medicines are useful in PCOS like Babuna, Nakhuna, Makoh, Revand khatai.

One female doctor given feedback that with the use of Flaxseed powder five gram BD, cleared PCOS in four months in two cases.

### Compound Formulations

- a. *Majoon Saras*
- b. *Majoon muqil hamwazan*
- c. *Majoon dabeedulward*
- d. *Majoon muqawwe reham*
- e. *Majoon falasifa*
- f. *Majoon supari pak*
- g. *Arq badiyan*
- h. *Arq zeera*
- i. *Habbe rasaut*
- j. *Habbe hilteeth*
- k. *Habbe hamal*
- l. *Dawaul kurkum*
- m. *Dawaul misk*
- n. *Safoof tabasheer*

### Diet and Exercise

a. Low carbohydrate, high protein, and high fat is useful in all types.

b. Gluten free diet is beneficial in all types.

c. All types of exercise give benefit in metabolic syndrome (*Sauda*)

d. All *Mudirrat e Haiz* are beneficial like Abhal, Ulat Kambal, Ashok, Tabasheer.

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