HYPERANDROGENISM IN FEMALE: A CRITICAL VIEW

Anupama M. Bathe¹, Puja M.Sansare², Ajay Kumar Sahu³, R.K.Joshi⁴

¹P.G. Scholar, ²Lecturer, ³Professor & HOD Department of Kaychikitsa, ⁴P.G.Scholar, Department of Rasashastra & Bhaishajya Kalpana, NIA, Jaipur, Rajasthan India

ABSTRACT

Androgen is male sex hormone secreted by adrenal cortex and ovaries in female. Androgenic disorders are the most common endocrinopathy of women of reproductive age, with prevalence of 10% - 20%. In this majority of patients with Androgen excess will have Polycystic ovary syndrome. The most common clinical manifestation of hyperandrogenism in women is persistent acne, hirsutism, androgenic alopecia. These causes physical & mental disturbance and loss of confidence which make women to hide from the world. Hyperandroginism is the gift of modern era, the exact disease related to Hyperandroginism was not mentioned in Ayurvedic literature. In this paper the attempt had been made to discuss causes, dosha- dashya involvement and pathogenesis of hyperandrogenism in female with respect to Ayurveda and according to that develop a treatment protocol to treat it.

Keywords: Hyperandrogenism, Hirsutism, Androgenic alopecia.

INTRODUCTION

Hyperandrogenism is the condition developed due to modernisation in day today life which may involve improper Dinacharya (Daily routine), Ritucharya also Rajaswalaparicharya (routine or do’s during menstruation and whole menstrual cycle), Garbhiniaparicharya (antenatal care or routine should be followed during pregnancy) etc. It is lifestyle disorder having hormonal imbalance. In comtemporary medicine Hyperandrogenism does not have exact treatment to treat and side-effect of that medicine are much more. So to treat this endocrinopathy of woman of reproductive age through Ayurveda one must know the exact causes, pathogenesis, and treatment of this disease given in modern science. Aacharya Charak has quoted that the physician should not worry about naming of particular disorders if it is not known to him. He should initiate treatment after assessing pathogenesis, location and etiological factors of the disorders.¹

Androgen²- An androgen is a substance having the capacity to produce masculinity. There are many of these, some occurring naturally and some produced artificially. All tend to be anabolics as well as sex determinants and there is a tendency to group them according to the dominant action. Testosteron is one of the most important androgen metabolised in the liver extremely rapidly and excreted from urine after degradation. Androgen conserves nitrogen and assist in the build up of protein. They also favour potassium, phosphorus and sulphur retention and for these reason important of muscle
and the growth of bone. They therefore bring about an increase in weight, promote muscular strength and energy, and give a sensation of well being. Androgen accelerates epiphyseal closure and ultimately limits stature; they also cause retention of sodium, chloride and fluid.

**Action of androgen in female**

**Atrophy of the tubes, vagina, vulva and breast**- Androgens directly depresses the activity of all the tissues of the female genital tract and induce atrophy and secretary quiescence of the lining epithelia. The breast shrinks, cervical secretion dries up and menstruation ceases.

Suppression of uterine and tubal contractions- These decrease both in frequency and in amplitude.

**Ovaries** –The ovarian cycle is arrested and ovulation and menstruation cease. This is a direct effect rather than one exerted through the hypothalamic-pituitary system.

**Secondary sexual characters**- Androgens are normally responsible for certain female sex characters as the axillary and pubic hairs, axillary sweating and activity of apocrine glands.

**Evaluation of Hyperandrogenism : Physical Examination**

Manifestations of androgen excess are typically evident with a detailed history and physical examination. The history should emphasize age of onset, timing of onset (gradual or rapid), and duration of symptoms, and menstrual history should be elicited to determine irregularities. Physical examination should include inspection of the skin, breasts, pelvis, and abdomen.

**Common Symptoms**

**Hirsutism**, excessive terminal (coarse) hair growth in androgen-dependent areas of the body, is the most common sign of hyperandrogenism, occurring in 60% to 80% of patients. Hirsutism should not be confused with hypertrichosis, which is defined as a diffuse increase in vellus (fine) hair growth.

**Virilization**, defined as the development of male characteristics in women, that is of rapid onset is generally a more ominous sign, suggesting the presence of an androgen-secreting ovarian or adrenal tumor. An estimated 5% to 10% of women in the general population are hirsute. However, prevalence rates of hirsutism depend somewhat on the scoring method used to determine its presence. Hatch and colleagues modified this scoring system to include 9 androgen-sensitive areas of the body. Each area is scored from 0 to 4 depending on the amount of terminal hair growth. A score of 8 or greater indicates the presence of hirsutism, although some experts recommend a score of 6 or greater.

**Acne** is a common manifestation of hyperandrogenism. Acne is characterized by increased sebum production, follicular epidermal hyperproliferation, proliferation of *Propionibacterium acnes*, and inflammation and occurs predominantly on the face and to a lesser extent on the back and chest. Androgens play a key role in the development of adult onset acne. Measurement of circulating androgens in patients presenting with adult onset acne and hirsutism is helpful for finding the underlying cause.

**Acanthosis nigricans** is characterized by areas of hyperpigmented, velvety plaques typically found in the axilla, neck, and groin areas and is found in patients with PCOS or type 2 diabetes mellitus. Its presence should prompt an evaluation for impaired glucose tolerance.

**LABORATORY EVALUATION**
Testosterone is the key circulating androgen; it is secreted directly from the adrenal glands and ovaries or produced through metabolism of androstenedione or DHEA-S in peripheral tissues. The normal testosterone level in women is less than 100 ng/dL. Free testosterone binds to tissue receptors, and measurement of free testosterone is 50% more sensitive for detecting androgen excess than total testosterone. The calculated free androgen index (FAI; total testosterone level divided by sex hormone–binding globulin [SHBG] level) can be used to estimate free testosterone and is a sensitive marker for detecting androgen excess. A ratio of less than 7 on the FAI is considered normal in women. Very high levels of total testosterone (> 200 ng/dL) or DHEA-S (> 700 μg/dL) can suggest an underlying neoplasm, but not all patients with these values will have a tumour.

CAUSES OF HYPERANDROGENISM

• Polycystic ovary syndrome
• Idiopathic hirsutism
• Hyperandrogenic insulin-resistant acanthosis nigricans (HAIRAN) syndrome
• Congenital adrenal hyperplasia (classic and non classic)
• Cushing’s syndrome
• Androgen-secreting tumors (ovarian, adrenal)
• Hyperprolactinemia
• Hypothyroidism
• Androgenic medications (eg, danazol)

Polycystic Ovary Syndrome

First described in 1935 by Stein and Leventhal, PCOS is the most common endocrine disorder in women of childbearing age, affecting 5% to 10% of women in this age-group. PCOS usually begins at puberty, and manifestations of PCOS include hirsutism, obesity, insulin resistance, acanthosis nigricans, and menstrual irregularities. PCOS is commonly associated with insulin resistance and hyperinsulinemia. Insulin stimulates secretion of androgens by ovarian theca cells and also inhibits SHBG production, which increases free androgens. Similarly, excess luteinizing hormone (LH) increases ovarian androgen secretion. An LH/follicle-stimulating hormone (FSH) ratio of greater than 2.5:1 is the classic pattern associated with PCOS. Because of decreased levels of FSH relative to LH, the ovarian granulosa cells cannot aromatize the androgens into estrogens. Although a finding of polycystic (multifollicular) ovaries on ultrasound is not solely diagnostic of PCOS, the presence of polycystic ovaries can strengthen the diagnosis. PCOS is, in fact, a syndrome—a collection of signs and features in which no single test is diagnostic. Diagnostic criteria for PCOS were established by the 2003 Rotterdam Consensus Workshop. PCOS can be diagnosed when 2 of the following features are present:

1. oligo- or anovulation,
2. Clinical and/or biochemical signs of hyperandrogenism (i.e., hirsutism, acne, male pattern balding, elevated Serum androgens), and
3. Polycystic ovaries.

It is important to exclude other disorders with a similar clinical presentation before a diagnosis of PCOS is made.
compared with all other diagnostic groups. As compared with women with PCOS, women with HAIRAN syndrome have a much greater degree of insulin resistance and hyperinsulinemia and a higher association with type 2 diabetes.

**Congenital Adrenal Hyperplasia**

Congenital adrenal hyperplasia (CAH) is the result of 21-hydroxylase deficiency. This enzyme defect leads to the accumulation of steroid precursors, which are subsequently converted to androgen (Figure 2). Classic CAH presents at birth with virilization of the female external genitalia, whereas late-onset (non classic) CAH is milder and typically does not present until early puberty. The symptoms of non classic CAH include premature pubarche, primary amenorrhea, menstrual dysfunction, hirsutism, acne, and infertility. This disease closely mimics PCOS; therefore, in a patient presenting with phenotypic features of PCOS, it is important to consider late-onset CAH in the differential diagnosis. Laboratory assessment is critical for the diagnosis of CAH. In adults, a 17-hydroxyprogesterone level greater than 200 ng/dL may be due to non classic CAH.

**Cushing’s syndrome**

Menstrual irregularities and hirsutism are common symptoms in women with Cushing’s syndrome, collectively occurring in 80% to 90% of patients. These symptoms are hallmark findings of PCOS and are not specific to Cushing’s syndrome. In the absence of multifollicular ovaries, PCOS may be differentiated from Cushing’s syndrome by the presence of central obesity, facial plethora, moon facies, and violaceous abdominal stria greater than 1 cm.

**Androgen-Secreting Tumors**

Although androgen-secreting tumors are rare (< 1% of patients), they must be excluded in women who develop hirsutism or signs of virilization, including increased muscle mass, breast atrophy, clitoromegaly, and deepening of the voice, over a short period of time. Elevated DHEA-S is seen in androgen-secreting adrenal tumors, while elevated testosterone is seen in both androgen-secreting adrenal and ovarian tumors.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Additional Findings</th>
<th>Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycystic ovary syndrome</td>
<td>Irregular menses, glucose intolerance, elevated blood pressure</td>
<td>Elevated insulin levels, multiple ovarian cysts on ultrasound</td>
</tr>
<tr>
<td>Hyperandrogenism with normal ovulation</td>
<td>Regular menses</td>
<td>Elevated androgen levels</td>
</tr>
<tr>
<td>Idiopathic hirsutism</td>
<td>Regular menses</td>
<td>Normal androgen levels</td>
</tr>
<tr>
<td>Hyperandrogenic insulin-resistant acanthosis nigricans (HAIRAN)</td>
<td>Acanthosis nigricans</td>
<td>Elevated fasting glucose and insulin levels</td>
</tr>
<tr>
<td>Late-onset congenital adrenal hyperplasia (nonclassic)</td>
<td>Short stature</td>
<td>Elevated 17-OH-progesterone</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia (21-hydroxylase deficiency)</td>
<td>1%</td>
<td>Possible virilisation</td>
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<tr>
<td>Hypothyroidism</td>
<td>&lt;1%</td>
<td>Fatigue, weight gain, amenorrhea</td>
</tr>
<tr>
<td>Cushing’s syndrome</td>
<td>&lt;1%</td>
<td>Abdominal striae, central obesity</td>
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</tbody>
</table>

So the above data suggest the pathology regarding androgen start from its origin of secretion that is from ovaries and adrenal gland but for maintenance of its proper level in blood, Liver (Cholesterol), pancreas (insulin) plays an important role. So the drugs have to be selected which normalise the function of above organs.

**Ayurveda and Hyperandrogenism**

Hyperandrogenism is the gift of modern era, so the exact disease related to Hyperandrogenism was not mentioned in Ayurvedic literature. It does not correlate the condition to a single disease but the symptoms bear a resemblance to the different terminologies in Ayurvedic classics. The symptoms of Hyperandrogenism may be correlated with Pushpaghni Revati having symptoms as Vritha pushpa (Anovulation), Sthula ganda (indirectly denotes obesity), Lomasha ganda (Hirsutism). Also as described above main cause of hyperandroge

<table>
<thead>
<tr>
<th>Vyadhi</th>
<th>Hetu</th>
<th>Lakshana</th>
<th>Contemporary symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pushpaghni Revati&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Improper lifestyle during pregnancy</td>
<td>Vritha pushpa Sthula ganda Lomasha ganda</td>
<td>Anovulation, obesity, Hirsutism</td>
</tr>
<tr>
<td>Arajaska Yonivyapad&lt;sup&gt;23&lt;/sup&gt;</td>
<td>Pittaprapakaaaharvihar</td>
<td>Shushkataof the Raja</td>
<td>1. An increased interval between two cycles. 2. Scanty menstrual flow</td>
</tr>
<tr>
<td>Lohitakshyaya</td>
<td>Vata-Pittapradhanaahar-vihar</td>
<td>Rajaksheenata</td>
<td>Scanty menstrual flow</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Yonivyapad(^{24})</th>
<th>Vataprakopakahetusevan</th>
<th>Yonirukshata</th>
<th>dryness of genital tract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shushka Yonivyapad(^{25})</td>
<td>Vata vitiation due to genetic factors</td>
<td></td>
<td>uterus, ovaries or the genital system itself is undeveloped.</td>
</tr>
<tr>
<td>Shandhi Yonivyapad(^{26})</td>
<td>Dhatukshaya</td>
<td>Nashtartava</td>
<td>loss of menstruation</td>
</tr>
<tr>
<td>Vandhya Yonivyapad(^{27})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abeejata(^{28,29})</td>
<td>frequent or untimely coitus, over-exercise, ruksha(dry), tikta(bitter), kasha(astringent), atilavana(excessively salty), amla(sour) and ushna(hot)aahar, as also chintalshoka (stress-related tension), bhaya(fear), krodha(anger) and aghatai.e.injuries due to shas tra(weapon)orkshara(alkali)</td>
<td>Artavaabeejata</td>
<td>Anovulation</td>
</tr>
<tr>
<td>Ashtartava Dushti(^{30})</td>
<td>Artava vitiated by the Doshas</td>
<td>Abeejata</td>
<td>anovulatory menstruation only</td>
</tr>
<tr>
<td>Rajodushthi(^{31})</td>
<td>vitiation of Raja by the Doshas, primarily Vata and Pitta</td>
<td>Ksheenata</td>
<td>Oligomenorrhoea</td>
</tr>
</tbody>
</table>

Considering all the above mentioned types of conditions/diseases quoted in the classics it can be noted that neither of them bears a complete resemblance to the current features of hyperandrogenism.

For the treatment of any disease through ayurveda one should know the Hetu (Cause)for Parivarjan (abstinence), Samprapti (Pathogenesis) for Samprapti vighatana (break down ), and Chikit-sasiddhanta (treatment principle).

**Hetu (Cause)**

Considering above mentioned condition it can state that it is a disease caused by vitiation of dosha during embryonic life or after birth by improper life style. *Beejadosha* (Genetic) may occurred due to improper Garbhini Paricharya (antenatal care) as Acharya Kashapa mentioned causes of Jatharini Revati as improper Ahar-Vihar (life style) during pregnancy. Pushaghni Revati has some symptoms related to Hyperandrogenism.

Vitiation of of Dosha after birth is due to improper life style means due to breaking rules told by Acharyas regarding Dinacharya, Ritucharya and most important for women i.e. Rajasvalaparicharya. In day today life there is increase burden of work...
causing stress which contributes to vitiation of ManasDosha (psychological factors) and ultimately leads to hormonal changes.

**Samprapti (Pathogenesis)**

By seeing above table, it is clear that this is the disease belongs to the category of Santorpannatha vikar (disease caused by overweight / nutrition). As an androgen is a substance having the capacity to produce masculinity so weight gain is mainly observed in patients of PCOD and other causes of Hyperandrogenism given above.

Vitiation of above factors occurs due to:

- **Agnimandya- Jatharagni & Dhatvagni**
  Agnimandya (decresce digestive power) is the key factor for production of any disease. Pitta is consider as Agni by Acharya Sushruta and Pitta is nothing but Bile from liver and Pancreatic secretions,. Formation and metabolism of hormones are at the level of Liver as Cholestrol is formed there which is responsible for production of androgen, regarding pancreatic secretion insulin alters the androgen secretion.

  The above stated aetiological factors give rise to Jatharagni (digestive power at stomach level) and Dhatvagnimandya (digestive power at cellular leval) along with Aamotpatti (end product fromed due to improper digestion) resulting in Medoroga viz. Sthaulya (obesity). Aamotpatti and Agnimandya cause an improper nourishment of the consecutive dhatus. Artava, being the saptamdhatu thus becomes ksheen (undernourished). The bulky appearance of the antaphala (ovaries) can be attributed to their vitiation by Kapha and Meda thus leading to an increase in the ovarian volume, which increases the secretion of the androgens and worsened the condition. Possible pathogenesis of ksheen artava is related with the vitiation of all the three dosha, but time period varies according to different phases of menstrual cycles. The vitiation of vata and pitta in first phase, affects the formation of endometrial thickness, where as the vitiation of kapha in second phase is responsible for the srotorodha (obstruction in channels). Thus the combined effect of all the three dosha creates the symptom of kheenartava.

  It can be stated that Kapha predominance manifests as obesity, subfertility, hirsutism, diabetic tendencies and hypothermia. Pitta predominance manifests as alopecia, acne, dysmenorrhea with clots and where as Vata predominance manifests with dysmenorrhea, oligomenorrhea and severe menstrual irregularity.

**Hyperandrogenism, the main pathogenesis occurs due to vitiation of Dosha**

- **Vata ( Apana,)**
- **Pitta ( Pachaka,Sadhaka)**
- **Kapha (Kledaka)**

**Dushya**

- **Dhatu-Rasa, Rakta, Shukra**
- **Upadhatu-Raja**

**Strotas-** Rasavaha, Raktavaha, medovaha & Manovaha Strotas

**Ayurvedic management of Hyperandrogenism-**

1. **NidanParivarjan (Abstinence of causative factors)**- It is first line of treatment in all types of diseases through Ayurveda. So the etiological factors responsible for pathogenesis of the disease should be excluded firstly.

**Etiological factors:**

- **1. Beejadoshaj (Genetic)**
- **2. Apathyanimitaj (Acquired due to improper life style)**
For the prevention of Beejadosha, Ayurveda mentioned the Shodhan therapy, which includes Panchakarma (helps in whole body detoxification, including Raja) before conception, whereas Garbhini-paricharya must be followed by female after conception.

Apathyanimitaj – Hyperandrogenism is life style disorder, so adaptation of proper life style through ayurveda i.e. Dinacharya, Ritucharya, & Rajaswala paricharya is mandatory.

2. Samprapti Vighatana (Break down of pathogenesis)-
As Hyperandrogenism comes under the category of Santarpanothena Vikar as mentioned above, so the prime line of treatment is Apatarpana which includes Shodhana and ShamanaChikitsa.

Shodhana (cleaning the body of abnormalities especially the doshas)-
1. Vamana (Emesis)- In Hyperandrogenism, the type of Strotadushti is of Sanga type, which is due to predominance of Kapha. And Vamana (emesis) is mainly prescribed for vitiated Kapha.

2. Virechana (Purgation)- Pitta is responsible for all the hormonal activities/secretion which maintains equilibrium of body. So, due to vitiated Pitta, excessive secretion of Androgen may occur. Virechana therapy is the prime treatment of Pitta dosha.
Also according to Ashraya-ashrayi Siddhanta, Pitta is ashrayi of Rakta, so vitiation of Pitta leads to vitiation of Rakta. And Rakta is transport medium of nutrition as well as hormone, enzymes etc. Acne, Acanthosinigricans which are symptoms of Hyperandrogenism is nothing but due to Pitta-Rakta vitiation also menstrual irregularities are also due to these dosha. Thats why Virechana along with Raktamokshana (expulsion of blood) may play principal role for normalisation of hormonal equilibrium.

3. Basti (Enema)- Excess Androgen secretion is from Ovaries and adrenal gland and these could be considered under Pakvashaya, which is seat of Vata Dosha and specially Apana Vata. Also Apana Vayu is the controller of all activities related to Dharan (hold) and Nishkramana (expelled) of Shukra-Artava.
The classics too quote Basti to be the modality of choice in this context due to its utility in conditions of vitiated Vata. Especially Anuvasan (enema with medicated oil), Niruha (enema with medicated decoction) and Uttarbasti (enema in the genital tract) which are more beneficial in this condition. The classics too quote Basti to be the modality of choice in this context due to its utility in conditions of vitiated Vata.

Shaman chikitsa (Suppression of abnormality at its place only)
In the menstrual disorders caused by Vatadi dosha, drugs suppressing that particular dosha should be used. Kashyapacharya quotes the use of Rasona (Allium cepa), Shatapushpa (Anethum graveolens) and Shatavari (Asparagus racemosus) to be beneficial in all disorders of Artava. He advocates the utility of Shatapurpakalpa (a formulation of Shatapursha) in the infertile woman to gain pregnancy. Also it belongs to Santorpannotha vikar so Apatartan (decresing the strength and weight) by Shaman should practice which may include Lekhaniya Mahakashaya, Mustadi Kwatha, Chikitsa siddhanta of Staulya, Prameha etc.

DISCOURSE &CONCLUSION-
Hyperandrogenism is a common endocrinopathy of women of reproductive age
which is life style disorder. It is not directly mentioned in Ayurvedic classics but from the pathogenesis and clinical manifestations of the hyperandrogenism, it is evident that it is Tridoshaja vyadh in which Rasavaha, Raktavaha, Medovaha & Manovaha strotasa are involved. Also it belongs to Santorpannothavikar so Apatarpan by Shodhana and Shaman & life style modification by practicing Dinacharya, Ritucharya, Rajasvala paricharya etc. should be done.

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CORRESPONDING AUTHOR
Dr. Anupama M. Bathe
P.G. Scholar, Department Of Kaychikitsa, NIA, Jaipur, Rajasthan, India
Email: dranupamabathe@gmail.com

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