

AYURVEDIC MANAGEMENT OF POLYCYSTIC OVARIAN SYNDROME (INFERTILITY QUEEN)

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Abstract : Polycystic ovarian syndrome/disease (Infertility Queen) is a systemic endocrine and metabolic disorder. It was originally considered a gynecological disorder. Hyperinsulinemia and hyperandrogenemia are the chief culprits responsible for oligo/amenorrhoea, hirsutism, obesity and enlarged ovaries with multiple small cysts and thick tunica results in anovulation. In Ayurveda few diseases in group of *yonī vyapad* and *jatiharini* have some similarities with this entity but *pushpaghni jatiharini* described by Acharya Kashyap has got much resemblance. Early recognition and intervention such as the development of further complications, medical and surgical treatment are advised according to need and severity of disease. Ayurveda advocate prevention of disease by following *dincharya* and *ritucharya*, by use of *pathya aahar*, *vihar*, *aushadh* and also by avoiding *apathya aahar*, *vihar*, *prajnaparadha*, *mandagni*, eating excessive sweet and *kaphvardhak aahar* and lack of love and other etiological factors. Therefore kapha reducing, insulin rebalancing, obstruction clearing *aushadh aahar* and *vihar* can help to prevent / treat PCOS. This disorder involves *pitta*, *kapha*, *medas* with *ambuvahasrotas* and *artavdhatu*, these should be considered during treatment.

Keywords: Polycystic ovarian syndrome (PCOS), *Yoni vyapad*, Serum hormone binding globulin, *Ritucharya*, *Dincharya*, Infertility, Infertility queen.

Introduction

Infertility Queen or Polycystic Ovarian Syndrome (PCOS) or disease is a systemic endocrine and metabolic disorder affecting approximately 10% of women of reproductive age with onset manifesting as early as puberty, previously known as Stein Leventhal Syndrome includes oligo/amenorrhoea, hirsutism, obesity and enlarged ovaries with multiple small cysts and thickened tunica (**Stein and Leventhal, 1935**).

Ayurveda, the ancient science has answer to many diseases including polycystic ovarian syndrome. As the name suggest it is group of many disorders hence a single *yonī-vyapad* or any single disease can not be correlated with this entity.

Incidence: At least 20% of young woman have polycystic ovary (**Polson et al., 1988; Clayton et al., 1992**). But one out of three have symptoms consistent with diagnosis of polycystic ovary disease i.e infertility, menstrual irregularity or hirsutism.

Etiopathogenesis :- The cause of the PCOS remain unknown, insulin resistance and hyperandrogenism play an important role. There is no defect in Hypothalamo-Pituitary-Ovarian axis but normal function is masked by inhibition of ovarian follicular development and inappropriate feedback to pituitary.

The high oestrogen production is largely due to conversion of androgen to estrogen in the ovary and peripherally. It causes increase in luteinizing hormone (LH) and decrease in

follicle stimulating hormone (FSH). A vicious circle is established for the increase in luteinizing hormone induces thecal hyperplasia and increased androgen synthesis in the ovary. High level of androgen results in increase in the peripheral production of the sex hormone binding globulin (SHBG). This leads to increased level of free androgens to produce hirsutism and to be converted to oestrogen. The hyperthecosis is related to an over production of androgens which reduces granulosa cell proliferation and maturation, as well as stimulating fibrosis of surrounding stroma and capsule resulting in anovulation and infertility (Jeffcoate's Principal of Gynaecology). **Burghen et al.** in 1980 first described the association between hyperinsulinemia and hyperandrogenism and stated that in addition to hirsutism and infertility PCOS has associated metabolic risks (**Burghen et al., 1980**). Another consequence of the raised estrogen level is the target organ effect on adipose tissue formation and endometrial hyperplasia, may result in endometrial cancer.

Now a days Genetic involvement in PCOS cases is emerging. The main steroidogenic genes that were reported to play a role in the pathogenesis of PCOS are CYP11a, CYP17 and CYP21 (**Aldo, 2005**) and follistatin gene (**Urbank et al., 1999**).

According to Ayurveda - It occurs due to *prajnaparadha*, *mandagni*, eating excessive sweet and *kapha* alleviating foods and lack of love.

Sign and Symptoms

Oligo/ Amenorrhoea, Anovulation and Infertility : These are due to increased level of endometrial and follicular activity, approximately 100% of patients with PCOS are considered to be oligo or anovulatory although not all the patients present with an overt abnormality in their cyclic menstrual bleeding pattern (**Ricardo et al., 2005**). A prospective study conducted on 400 unselected women of general population

nearly 60% had menstrual dysfunction (**Azziz et al., 2004**).

Hyperthecosis is related to overproduction of androgen which reduce granulosa cell proliferation and maturation and stimulate fibrosis of surrounding stroma and capsule. Ovulation may occur intermittently.

The elevated LH levels, deficient progesterone secretion, abnormal embryo from atretic oocytes and abnormal endometrium could be some of the reasons attributed to pregnancy loss (**Enrico and Rogerio, 1999**).

Obesity:

It is one of the features of the original description of the syndrome by Stein and Leventhal, is seen in 35-60% of women with PCOS (**Balen et al., 1995**). Typically this obesity is centripetal, related to truncal abdomen for distraction demonstrated by an increased waist to hip ratio (**Evans et al., 1988; Pasquali et al., 1993**). Obesity is a cause of PCOS or it is result of PCOS is unclear, but it seem that later is more likely (**Samuels Thatcher**). Woman with central fat have high level of LH androsteindione, estrone, insulin, triglycerides, very low density lipoproteins (VLDL and lower level of high density lipoproteins (HDL) (**Pettigrew et al., 1997**).

Mitchell and Rogers reported that obesity was present at four times higher than woman with normal cycles (**Mitchell, 1953**).

Hirsute:

Excess terminal body hair has in a male distribution pattern commonly seen in upper lip, chin and along with linea alba of lower abdomen, may have acne, male pattern balding, hirsute effects psychological life of woman. The treatment of hirsutism embraces both cosmetic and hormonal therapies.

Androgenic Alopecia:

Loss of scalp terminal hair that is common with baldness, it is seen in PCOS woman (**Futterweit et al., 1988**).

Acne:

Very common and good indication of hyperandrogenism, present in one third of PCOS women.

Acanthosis Nigricans:

Mucocutaneous pigmented eruption typically found on posterior neck, axilla, mammary folds.

Hyperandrogenism:

Upto 70% of patients have elevated androgen level and other 30% patients in the high range (**Theresa et al., 2003**). The excretion of dehydroepiandrosterone and exclusive adrenal steroid is elevated in upto 50% of all woman with PCOS. The primary androgen raised in PCOS in the ovary include testosterone and androstenedione and the products will not be suppressed by adrenal steroid but by gonadotrophins releasing hormone agonists.

Hyperinsulinemia:

Insulin resistance accompanied by compensating hyperinsulinemia (elevated fasting blood insulin level) are important biochemical feature of PCOS. Hyperinsulinemia increases ovarian androgen production (particularly testosterone and androstenedione) and decreases the sex hormone binding globulin (SHBG) concentration (**Keri, 2001**).

Long Term Implication:

1. Diabetes: 20% of women with PCOS develops noninsulin dependent diabetes (NIDDM) by the age of 30 years. Women diagnosed having PCOS before pregnancy have an increased risk of development of gestational diabetes (Royal college of Obstetrician and Gynecologist, May, 2003).

2. Cardio Vascular Risk: In women with PCOS central obesity insulin resistance and hyperlipidemia constitute the bases for an increase in Cardio vascular risk (<http://herkules.oulu.fi/isbn9514264266/html/x891.html>).

3. Bone Mineral Density: There is definite positive correlation between androgen

levels and bone mineral density. This chronic elevation in androgens may exert a positive influence on bone in women with PCOS; either directly through androgen receptors on bone related cells or indirectly after conversion to 17- β estradiol and estrone respectively in peripheral tissue. Moreover, elevated circulating insulin levels also associated with PCOS, may offer some additional protection against a reduction in bone mass in these women (**Jeanne et al., 2000**).

4. Risk of Cancer (endometrial and ovarian): Due to unopposed effect of estrogen in the endometrium lack of cyclical progesterone allow for endometrial growth. Endometrial cancer in women under 40 years of age is rare with a reported incidence of 1-8% (**Eva, 2000**). Ovarian cancer is also increased 2-3 folds in women with PCOS.

Acanthosis Nigricans: Brownish / black velvety pigmentation of the skin most commonly seen at the base of neck Acanthosis a marker (A red flag) for insulin resistance ([http://www.whatreallywork.co.uk/start/ayurvediczone.asp?article/ID 1345](http://www.whatreallywork.co.uk/start/ayurvediczone.asp?article/ID%201345)).

Differential Diagnosis: Any process capable of producing acyclical estrogen production will produce clinical and endocrine features resembling the PCOS like.

- i. Cushing Syndrome.
- ii. Androgen producing tumor of the adrenal gland or ovary.
- iii. Congenital adrenal hyperplasia.

But for the diagnosis of PCOS, minimum three criteria has to be fulfilled.

1. Menstrual irregularity.
2. Hyperandrogenism: Shown clinically by hirsutism, acne, male pattern baldness, bio chemically by elevated serum androgen level.

3. Hyperinsulinemia (developed due to insulin resistance) elevated fasting blood insulin level.

Investigation and Diagnostic tests required

Despite the many symptoms associated with PCOS many woman are unaware that they have PCOS. Affected population is diagnosed during evaluation for irregular menstruation/ amenorrhoea, infertility, obesity and for hirsute following tests will be required to diagnose the cause and to decide its severity

1. Complete Hormone Profile (LH, FSH, total testosterone, androstenedione, estradiol) Estrogen and follicular stimulating hormone (FSH) are normal and as result there is an increase in LH:FSH ratio (1.5 to 3 time) (**Jacobs et al., 2001**) and LH surge is absent. It has been reported that 75% of woman with clinical evidence of PCOS have a elevated LH level and 94% has increased LH/FSH ratio (**Rendall et al.**).
2. Fasting blood insulin level- it is elevated.
3. Increase level of very low density lipoprotein (VLDL), decrease level of high density lipoprotein (HDL) or good cholesterol.
4. Ultrasound featuring thickened capsule of ovary with numerous small cyst in ovarian cortex. In Europe greater emphasis has been placed in ultrasound diagnosis of polycystic ovary, while in North America it did not include ultrasound feature.
5. Colour Flow Doppler.
6. Magnetic resonance imaging (MRI).
7. CT abdomen.

In the same way some of *yoni vyapad* and few another disorder can be compared with PCOS and other disease resemble with PCOS.

PCOS in Ayurveda

i. *Shandi Yoni Vyapad* (C.S.)

“*Bijdoshattu garbha sthmarutophatshya. Nradweshinyastani chaiv shandi syadanupkramah*” (C.S.Ch. 30/34-35)

- > A congenial disorder (*bijadosha*).
- > Absence or slight development of breasts.
- > Dislike coitus.
- > Incurable Disease.

ii. *Shandi Yoni Vyapad* (S.S.)

“*Anartavstna shandi kharsparsha cha maithune. Chasrashvapi chadhyasu sarvlingochhitirbhavet*” (S.S.Ut. 38/18-20).

- > Primary amenorrhoea (*anartava*).
- > No breast development (*astana*).
- > Capable of coitus but vaginal canal is rough.

iii. *Bandhya*

“*Yada hyasyah shonite garbha shyabeejbhagah pradoshmapadyate. Tada bandhyam janyati*” (C.S.Sh. 4/30).

Bijamsa dushti (chromosomal /genetic abnormalities); if part of *bija* responsible for the development of uterus is defective then born girl child would be *bandhya* (infertile)

iv. *Bandhya Yoni Vyapad*

“*Bandhyam nashtartvam vidhyat chashrastpichadyasu bhavantyanilvednah*” (S.S.Ut. 38/10-11).

- > Breast developed (only differentiating point with *shandi*).
- > Has amenorrhoea (*nastratava* considered as destruction of *artava* of female foetus).

v. **Vikuta Jatiharini**

“Kalvarnapramanerya vishmam
pushpamrichhati.

Animittbalglanirvikuta nam sa
smrita” (Ka.S.K. 6/34-35).

- > Oligomenorrhoea and scanty menses or excessive menses.
- > General weakness (metabolic manifestation).

vi. **Pushpaghni Jatiharini**

“Vritha pushpam tu yo nri yathakal
prapashyati. Sthulalomashganda
vpushpaghni sa api revati”
(Ka S.K.6/32-33).

- > It is curable.
- > woman menstruate in time but it is useless (vyathpushpa i.e anovulatory cycle).
- > Has corpulent and hairy cheeks – hirsutism; may be due to hyperandrogenism.

Thus *Pushpaghni jatiharini* seems to be nearer to polycystic ovary syndrome.

- > *Sthula purusha* (obese person) in *ashtanindiya* (censurable person) described by **Acharya Charak** have described 8 faults which include polyuria, polydipsia and short life. This condition may simulate with hyper insulinemia condition.
- > *Atiloma* person with excessive hair growth is also a censurable person.

Above two conditions may indicate female afflicted with PCOS.

Management

In modern medicine PCOS can be treated by following methods.

(A) Medical treatment:

1. Insulin Sensitizing Drugs

i. Metformin:

- > Enhances peripheral tissue sensitivity to insulin.

- > Inhibits hepatic gluconeogenesis.
- > An effect on increasing uptake and utilization of glucose by muscles.
- (ii) Thiazolidinediones: Troglitazone (due to suspected hepato toxicity it is withdrawn), D- Chiro – Inositol, Rosiglitazone Priglitazone.

2. Ovulation Inducer:

- (i) Clomiphene Citrate: Raises circulatory concentration of FSH.
- (ii) Gonadotrophin: LH alone/FSH alone / LH-FSH both.

Due to high sensitivity of polycystic ovary to gonadotrophins, it induces multiple follicular development there may be high frequency of ovary hyperstimulation syndrome (OHSS).

- (iii) Oral Contraceptive: Suppression of LH occurs due to which ovarian production of LH-dependent androgen is reduced and adrenal production of androgen is also decreased.

SHBG increased so that androgen does not wonder freely.

(B) Surgical treatment:

- (i) Wedge resection of the ovaries: Procedure is associated with high percentage of ovarian and periaidenexal adhesion, substantial tissue loss and premature ovaries failure of vasculature of ovary is disturbed (**Stein et al., 1935**).
- (ii) Ovarian drilling: Can be done laproscopically by making small holes in the ovarian coating capsule with a laser cautery needle.

(C) Hirsute: Can be treated by use of depilatory aids and electrolysis but the presence of body hair, acne and alopecia may also be respond to anti androgens such as cyprosterone acetate combined with an estrogen such as ethinyl estrogen given on a cyclical basis.

(D) Weight reduction: by life style modification and physical exercise.

Above mentioned management vary according to the need. Treatment can be divided into two groups:

- (a) PCOS woman want fertility: weight reduction + insulin sensitizing drugs with ovulation inducing drugs. Hirsutism can be treated with electrolysis /de-epilatory aids.
- (b) PCOS woman not bothred about fertility: weight reduction + oral contraception can used along with electrolysis or de-epilatory aids.

Some points for concern before discussing Ayurvedic Management

- > Now a days sedentary lifestyle, fast food, mental stress is responsible for obesity.
- > In a school the incidence of obesity was observed as high as 30% in cities in a recent survey. Normally in young Indian girls there is very little stress on physical activities.
- > Increase in BMI from 18 to 30 kg/m² is generally associated with PCOS.
- > Adipose tissue is an active site for steroid production and metabolism. It can convert androgen to estrogen, estradiol to estrone and DHEA to androstenediol (Pasquali *et al.*, 1993).
- > Weight loss promotes ovulation and fertility and reduces hirsutism (Marilyn, 2003).

Ayurvedic Management

Authors of today's modern science conclude their talk about PCOS with that - Early recognition and intervention, such as weight control, diet and lifestyle modifications may prevent / delay the development of further complications of PCOS. Ayurveda, the science of life starts with the quote

“Swasthasya swasthya rakshanam
aaturasya vikar prashmanam cha”
(Ch.Su. 30).

PCOS seems to be a disorder involving *vata, pitta, kapha, medas, ambuvahasrotas, artava dhatu*. So these all need to be considered in treatment.

PCOS can be prevented / treated with the help of *aahar, vihar* and *aushadh*.

1. Aahar and Vihar

- Balanced diet is essential for normal health. Because dietetic abnormality vitiate *doshas* which cause various gynecological disease may result infertility. It also produce loss of *dhatu* which influences hormones causes menstrual irregularity. Abnormal diet hamper nourishment of fertilized egg and implantation of zygote.
- Weight reduction by *pathya / apathya aahar* and *vihar*.
- Mode of life as suggested in the *ritucharya* and *dincharya* should be followed properly.
- Following are some *yoga* techniques helpful for weight reduction and to decrease blood sugar level as well. Like: Anuloma-Viloma, Kapalbhathi and Mandukasan. *Vyayam* (exercise) enhances tissue sensitivity to insulin (80% of the body's insulin mediated glucose uptake occurs in muscles).

2. Aushadh

- Kapha* reducing, insulin enhancing, hormone rebalancing, obstruction clearing herbs like Gurmar, Jambu, Tarwar, Guduchi, Amala and Haridra etc. are useful.
- > Kanchnar Guggal- being *ruksh* in *guna* old Guggal and Kanchnar both decrease fat due to *lekhan* action. They are *vata-kapha shamak* and *pitta kapha shamak* respectively.
- > Methi (Fenugreek - *Trigonella foenum graecum*) - reduces fasting blood sugar.

- > Karela (Bittergourd - *Momordica charantia*)- reduces fasting and post prandial blood sugar and appears to enhance tissue sensitivity to insulin.
- > Ashwagandha (*Withania somnifera*)- helps to reduce stress of amenorrhoea and infertility.
- > Shatawari (*Asparagus racemosus*) to bring balance and strength to the menstrual system.
- > Marich (Black pepper - *Piper nigrum*) - high in chromium (chromium picolinate 200-400 mcg /day (an anti oxidant) can assist in balancing blood sugar level.

Basti- Women having amenorrhoea, scanty menses, non ovulation or useless ovulation, cases of repeated abortion should be prescribed *anuwasana basti* (**K.S.Si 1/39-41**). *Yapana basti* perform both the action i.e. cleansing and oleation, so infertile couple get progeny (**C.S.Si. 12/20,22**). e.g. *satvaryadi anuvasana basti*, *guduchyadi rasayana basti* etc.

Summary

- > PCOS is a highly complex endocrine disorder.
- > It is a leading cause of infertility, menstrual disturbance and is associated with obesity, hirsutism and chronic anovulation.
- > PCOS can't be correlated with a single entity in ayurveda but has some resemblance with *pushpaghni jatiharini*. Others are *shandi yoni vyapad*, *bandhya* of **Charak**, *bandhya yoni vyapad* of **Sushruta**, *vikuta jatiharini* of **Kashyap**.
- > Obesity is the main cause and symptom which can be prevented by following *dincharya* and *ritucharya* and can be reduce by *pathya aahar*, *vihar*, *aushadh* and restriction of *apathya aahar vihar*.

Conclusion

To treat a woman affected with PCOS need controlled and balanced diet and exercise for weight reduction along with medication, preventive measures are more important. So it will be more beneficial to follow mode of life as mentioned in Ayurveda and to use modern medicine, if needed, to get conceived.

References

1. **Aldo E Caloegero**. Genetics of Polycytic ovarian syndrome. *Reprod Biomed Online* 10 (6) :71320 (2005).
2. **Ashtanga Sangraha**. Translated by Atridev Gupta, Published by Nirnaya Sagar Press, Bombay, first edition, (1951).
3. **Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES and Vildiz BD**. The prevalence and feature of the polycystic ovary syndrome in an un selected population. *J. Clin. Endocrinal Metabolism* 89;2745-2749 (2004).
4. **Balen A.H., Conway G.S., Kaltsas G., Techatrasak K., Manning P.J., West C. and Jacobs H.S**. Polycystic ovary syndrome; The spectrum of the disorder in 1941 patients. *Human Reproduction* 10,2107-2111 (1995).
5. **Burghen C.A., Givens J.R. and Kitabchi A.E**. Correlation of hyper and regemism with hyperinsulinamia in Polycystic ovarian disease. *Journal of Clinical Endocrinology and Metabolism* 50, 113-116 (1980).
6. **Charak Samhita** (Text with english translation and critical exposition based on Chakrapani Datt's Ayurved Dipika) by R.K Sharma, Bhagwan Das, Published by Chowkhamba Sanskrit Series office, Varanasi (1995).
7. **Clayton R.N., Ogdan V., Hodgkinyeson J., Worswick L., Rodini D.A. and Dyer Sand Meade T.W**. *Clin.Endocrin.* 37, 127-134 (1992).
8. **Enrico Carmina and Rogerio Aloba**. PCOS; Arguably the most common endrocrinopathy associated with significant morbidity in women. *The Journal of Clin. Endocrin.and Metabolism* 84: 1897-1899 (1999).
9. **Eva Dahlgren and Per Olof Janson**. Long Term health implication for women with polycystic ovary syndrome, In: Polycystic ovary syndrome, Cambridge University Press. Edited by Gaber T. Kovacs (2000).
10. **Evans D.J., Barth, J.H and Burke C.W**. Body fat topography in women with androgen excess. *International Journal of Obesity* 12,157-162 (1988).
11. **Futterweit W, Dunaif A, Veh C and Kingley P**. The Perspective of hyperandrogenism in 109 conductive female patients with diffuse alopecia *J. Med. Acad. Dermatol.* 19-831-36 (1988).

12. http://herkules.0414.fi/isbn9514264266/html_x891.html. *Endocrine and Metabolic changes in women with Polycystic ovary and with polycystic ovary syndrome*. Ritta Koivynan. Department of Obstetrics and Gynecology; University of Ohio (2001).
13. <http://www.whatreallywork.co.uk/start/ayurvedizone.asp> article ID=1345.
14. **Jacobs DS, DeMott WR and Oxley DK.** Luteinizing hormone, blood, and urine. Jacobs and DeMott laboratory test handbook, fifth edition, Hudson: Lexi-Comp Inc; pp 219-20 (2001).
15. **Jeanne V. Zborowski, Jane A et.al.** Bone mineral density, androgens, and the polycystic ovary: The complex and controversial issue of androgenic influence in female bone. *The Journal of Clinical Endocrinology and Metabolism* Vol 85:3496-3506 (2000).
16. *Jeffcoate's Principal of Gynecology*. revised and updated international edition by Arnold (2001).
17. **Kashyap Samhita.** Satyapal Bhisagacharya, Published by C.S.S. Varanasi, first edition (1953).
18. **Keri Marshall.** Polycystic ovary syndrome; clinical consideration. *Alter. Med. Rev.* 6(3) : 272-272 (2001).
19. **Marilyn R Richardson.** Current perspective in PCOS. *Am. Fam. Physician.* 68:697- 704 (2003).
20. **Mitchell. G.W and Rogers J.** The influence of weight reduction on amenorrhoea in obese women. *New England Journal of Medicine* 249; 635-7 (1953).
21. **Pasquali R, Casimirri F and Vicennati F.** Weight control and its beneficial effect on fertility in women with obesity and polycystic ovary syndrome. *Human Reproduction* 12 (suppl 1):827 (1997).
22. **Pasquali R., Casimirri F, Canlobelli S., Labate A.M. Venturoli S., Pradisi R. and Zannarini L.** Insuline and androgen relationships with abdominal body fat distribution in woman with and without hyperandrogenism. *Human Research* 39, 179 -187 (1993).
23. **Pettigrew R and Hamilton Fairley D.** Obesity and female reproductive function. *British Medical Bulletin* 53;341-58 (1997).
24. **Polson D. W, Adams J., Wadsworth J and Franks S.** Polycystic ovaries – a common finding in normal woman. *Lancet* 1, 870-872 (1988).
25. **Randall B Barnes, Adrienne B. Neithardt, and Suleena Kaha:** Hyperandrogenism. Hirsulism and polycystic ovary syndrome. Chapter 6 in ; *Female reproductive endocrinology*. www.endotext.org.
26. **Ricardo Azziz, Catherine Marine, Lalima Hoq Enkhe Badamagarob and Poul Song.** Health Care related economic burdern of the polycystic ovary syndrome during the reproductive life span. *The Journal of Clinical Endocrinology and Metabolism* 90(8) 4650-4658 (2005).
27. *Royal College of obstetrician and Gynecologist.* Long term consequences of polycystic ovary syndrome. Guideline no 33; May, 2003, 1-8 (2003).
28. **Samuel S. Thatcher.** What is Polycystic ovarian syndrome (PCOS) A fact sheet from the centre for applied reproductive science, www.obgyn.net / PCOS/ articles.
29. **Stein I.F and Levanthal M.L.** Amenorrhoea associated with bilateral polycystic ovaries. *American Journal of Obstetrics and Gynecology* 29, 181-191 (1935).
30. **Sushruta Samhita.** Dalhana Nibandha Sangrah commentary, Edited by Yadav ji Trikrimji Achrya, Published by Chowkambha Sur Bharati Prakashan, Varanasi (1994).
31. **Theresa L Max and Adv. E.Mehta:** Polycystic ovary syndrome : Pathogenesis and treatment over the short and long term. *Cleveland Clinic. Journal of Medicine* Vol 70 ; 31-45 (2003).
32. **Urbanek M, Legro and Driscoll D A et al.** Thirty seven candidate genes for polycystic ovary syndrome: strongest evidence for a linkage is with follistatin. *Proc. Natl. Acad. Sci. USA.* 96 : 8573-8 (1999).