WORLD JOURNAL OF PHARMACEUTICAL RESEARCH

SJIF Impact Factor 8.084

Volume 11, Issue 3, 384-395.

Review Article

ISSN 2277- 7105

MANAGEMENT OF POLYCYSTIC OVARIAN DISEASE THROUGH AYURVEDA: A REVIEW

Dr. Megha Bahuguna^{1*} and Dr. Shivam Vaidh²

¹Assistant Professor, Department of Rachna Sharir, Dev Bhoomi Medical College of Ayurveda and Hospital, Manduwala, Dehradun.

²Assistant Professor, Department of Kriya Sharir, Uttaranchal Ayurvedic Medical College and Hospital, Rajpur Road, Dehradun.

Article Received on 26 December 2021.

Revised on 15 Jan. 2022, Accepted on 04 Feb. 2022

DOI: 10.20959/wjpr20223-23162

*Corresponding Author Dr. Megha Bahuguna Assistant Professor, Department of Rachna Sharir, Dev Bhoomi Medical College of Ayurveda and Hospital, Manduwala, Dehradun.

ABSTRACT

Polycystic ovarian disease is a endocrine and metabolic disorder, which is very common now-a-days. It is not merely a gynecological disease, but can be considered as lifestyle disorder. Hyperinsulinemia and hyperandrogenemia are the main factors responsible for problems related to menstruation, hirsutism, obesity and ovarian enlargement with multiple small cysts and increase in thickness of tunica layer resulting in anovulation. In Ayurveda, yoni vyapad and jatiharini are mentioned as a group of female diseases and the symptoms mentioned there have some similarities with PCOD but pushpaghni jatiharini described by Acharya Kashyap has got much resemblance with its main clinical features. Ayurveda has its prior objective of preventing the 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 other etiological factors. Therefore kapha shaman, sroto shodhak aushadh- aahar and vihar can help to prevent / treat PCOD. This disorder involves pitta, kapha, medas with ambuvahasrotas and artavdhatu, which are primarily considered during treatment. This article deals with effect of hirak bhasma, tamra bhasma and abharak bhasma in the management of PCOD with reference to yonivyapad.

KEYWORDS: Polycystic Ovarian Syndrome (PCOS), PCOD, Yoni Vyapad, Hirsutism, Ritucharya, Dincharya, Infertility, Oligomenorrhoea, Hirak Bhasma, Tamra Bhasma, Abharak Bhasma.

INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) or disease is an endocrine and metabolic disorder affecting approximately 10-15% of women in their reproductive age with onset manifesting as early as puberty. It was previously known as Stein Leventhal Syndrome. The main symptoms of PCOD are oligo/amenorrhoea, hirsutism, obesity and enlarged ovaries with multiple small cysts and thickened tunica (Stein and Leventhal, 1935). Ayurveda, the ancient science has proved management for many diseases including polycystic ovarian syndrome/disease. As the name suggests, it is a group of many diseases, hence a single yonivapad or any single disease can not be corelated with this.

Incidence: At least 20% of women have polycystic ovarian disease.^[2] But only one out of three have consistent symptoms with diagnosis of polycystic ovary disease i.e infertility, menstrual irregularity or hirsutism.

Etiopathogenesis:- The cause of PCOD is still unknown in modern science, but insulin resistance and hyperandrogenism play an important role for its occurence. There is no significant abnormality seen in Hypothalamo-Pituitary Ovarian axis but normal function is affected by inhibition of ovarian follicular development and maturation which gives inappropriate feedback to pituitary. The high oestrogen production is mainly 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 increased luteinizing hormone which induces thecal hyperplasia and increased androgen synthesis in the ovaries. When levels of androgens become high, they result in increase in the peripheral production of the sex hormone binding globulin (SHBG). Due to which free androgens levels increase to produce hirsutism and to be converted to oestrogen. An over production of androgens which decreases granulosa cell proliferation and maturation, then causes hyperthecosis, as well as stimulating fibrosis of surrounding stroma and capsule resulting in an anovulatory cycle and infertility (Jeffcoate's Principal of Gynaecology), first described the relation between hyperinsulinemia and hyperandrogenism and stated that along with hirsutism and infertility, some metabolic risks are also associated with PCOD. [3] Another consequence of the high estrogen level is its effect on target organ adipose tissue formation and endometrial hyperplasia, which may result in endometrial cancer. Now a days, Genetic involvement in PCOD cases is also seen. The main sterroidogenetic genes that were reported to play an important role in the pathogenesis of

PCOD are CYPlla, CYP17 and CYP21 and follistatin gene. [4] In Ayurveda, there are well explained causes of PCOD - It occurs due to prajnaparadha, mandagni, eating excessive sweet and kapha alleviating foods and emotional factors. [5] Sign and Symptoms, like Oligo/ Amerorrhoea, Anovulatory cycle and Infertility are due to increased level of endometrial and follicular activity, approximately 100% of patients with PCOD are seen with oligomenorrhoea or anovulatory cycle, although not all the patients present with an over abnormalily in their cyclic menstrual bleeding pattern. [6] A prospective study conducted on 400 unselected women of common population nearly 60% had menstrual dysfunction. [7] Hyperthecosis is associated with overproduction of androgen which reduces granulosa cell proliferation and maturation and stimulate fibrosis of surrounding stoma and capsule. Ovulation may occur intermittently. The elevated LH levels, deficient progesterone secretion, abnormal embryo from atritic oocytes and abnormal endometrium can be considered as some of the reasons attributed to pregnancy loss.^[8]

- 1. 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. [9] Typically this obesity is centripetal, related to truncal abdomen for distraction demonstrated by an increased waist to hip ratio. [10] Obesity is a cause of PCOS or it is result of PCOS is unclear, but it seem that later is more likely. [11] 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). [12] Mitchell and Rogers reported that obesity was present at four times higher than woman with normal cycles.^[13]
- 2. Hirsutism: Excess terminal body 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.
- **3.** Androgenic Alopecia: Loss of scalp terminal hair that is common with baldness, it is seen in PCOS woman.^[14] 35 Infertility Queen 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 17β estradiol and esterone 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.^[15]

- **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%. [16] Ovarian cancer is also increased 2-3 folds in women with PCOS.
- **5.** Acanthosis Nigricans: Brownish / black velvetty pigmentation of the skin most commonly seen at the base of neck Acanthosis a marker (A red flag) for insulin resistance.

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

- 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. 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. [17] 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 compansating 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. [18]

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. [19]

- 2. Cardio Vascular Risk: In women with PCOS central obesity insulin resistance and hyperlipidemia constitute the bases for an increase in Cardio vascular risk. [20]
- 3. Bone Mineral Density: There is definite positive correlation between androgen 36 Mishra and Sinha 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 testrosterone, 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)[21] 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. [22]
- 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

- Shandi Yoni-Vyapad (CHARAK SAMHITA) "Beejdoshatu garbhasthamarutophatshya. Nradweshinyastaani cha ev shandi syad anupkramah^[23]".
- congential disease (beejadosha).
- Under developed or absent breasts.
- Not like to do coitus.
- Incurable Disease.

- ii. Shandi Yoni-Vyapad (SUSHRUT SAMHITA) "Anartavastna shandi kharsparsha cha maithune. Chasrashvapi chadhyasu sarvlingochhitirbhavet" [24] (Su.Sa.Ut. 38/18-20).
- Primary amenorrhoea (anartava).
- No development of breasts (astana).
- Capable of coitus but vaginal canal is rough.
- iii. Bandhya "Yada hi asyah shonite garbha shyabeejbhagah pradoshmapadyate. Tada bandhyam janyati" (Ch.Sa.Sh. 4/30).

Beejamsa dushti (chromosomal /genetic abnormalities); if part of *beeja* 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 (nast-artava considered as destruction of artava of female foetus).
- v. Vikuta Jatiharini "Kalvarnapramanerya vishmam pushpamrichhati.

 Animittbalglanirvikuta nam sa smrita".^[27]
- Oligomanorrhoea 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". [28]
- 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 discribed 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 – Inositrol, Rosiglitazone Priglitazone.

- 2. Ovulation Inducer: (i) Clomiphene Citrate: Raises circulatory concentration of FSH. (ii) Gonadotrophin: LH alone/FSH alone / LHFSH both. Due to high sensitivety of polycystic ovary to gonadotrophins, it induces multiple follicular developments there may be high frequency of overy hyperstimulaton 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 periadenexal adhesion, substantial tissue loss and premature ovaries failure of vasculature of ovary is disturbed. [29]
- (ii) Ovarian drilling: Can be done laproscopically by making small holes in the ovarian coating capsule with a laser cautary needle.
- (C) Hirsute: Can be treated by use of deepilatory 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 use along with electrolysis or deepilatory 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. [30] > Weight loss promotes ovulation and fertility and reduces hirsutism.^[31]

Ayurvedic Management

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". [32] 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*, all together.

- 1. Aahar and Vihar(food and lifestyle) -Healthy and Balanced diet is essential for normal health. Because dietetic abnormality vitiate doshas which cause various diseases, may result in gynaecological problems and even infertility. It also produces condition of dhatu kshaya(loss of dhatu) which influences hormones causes menstrual irregularity. Abnormal diet disturbs nourishment and maturation of fertilized egg and implantation of the 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: AnulomaViloma, Kapalbhati 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 aushadh 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 vatakapha 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.

Ras Aushadh- Heerak bhasma-tridosh shamak, sampoorna rognashak, utkrisht rasayan etc. and acts as shoth har, kaf pitt roghar^[33,34] Tamra bhasma-pittkafhar, lekhan karma^[35], shat puti and sehesra puti Abhrak bhasm-amrit tulya, rasayan, vajikar, kafnashak, sampoorna rog nashak, santanotpadak^[36] etc.

3. Shodhan

Basti- Women having amenorrhoea, scanty menses, non ovulution or useless ovulation, cases of repeated abortion should be prescribed *anuwasana basti*. [37]

Yapana basti perform both the action i.e. cleansing and oleation, so infertile couple get progeny. [38] e.g. satvaryadi anuvasana basti, guduchyadi rasayana basti etc.

Uttar basti is also very beneficial.

CONCLUSION

To treat a woman with symptoms of PCOS, need to follow controlled and balanced diet and physical work out along with medication; moreover, preventive measures are very important. So it will be very beneficial to follow *Dincharya* and whole lifestyle as mentioned in Ayurveda.

In this study, we have tried to inculcate and study the management part described in ayurveda classics for the signs and symptoms relating with PCOS. Here, we found to have high success rates when we used *Ras aushadhis* in our *shaman chikitsa along* with *shodhan karma*. Use of *Heerak Bhasm*, *Abhrak Bhasma* and *Tamra Bhasma* in such patients proved to be most effective part of the management of PCOS.

REFERENCES

- 1. Aldo E Caloegero. Genetics of Polycytic ovarian syndrome. Reproductive Bio Medicine Online, No 6. 2005; 713–720 Article/1644 on web 4 April 2005.
- 2. R. N. Clayton, How common are polycystic ovaries in normal women and what is their significance for the fertility of the population?, Clinical Endocrinology, Volume-37, Issue 2, August 1992.
- 3. Burghen GA, Givens JR and Kitabchi AE (1980) Correlation of hyperandrogenism with hyperinsulinism in polycystic ovarian disease. *J Clin Endocrinol Metab*, 50: 113–116.
- 4. Aldo E Caloegero. Genetics of Polycytic ovarian syndrome. Reproductive BioMedicine Online; No 6. 2005; 713–720 Article/1644 on web 4 April 2005.

- 5. Ashtanga Sangraha. Translated by Atridev Gupta, Published by Nirnaya Sagar Press, Bombay, first edition, (1951).
- 6. 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, 2005; 90(8): 4650-4658.
- 7. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES and Vildiz BD. The prevelance and feature of the polycystic ovary syndrome in an un selected population. J. Clin. Endocrinal Metabolism, 2004; 89: 2745-2749.
- 8. Enrico Carmina and Rogerio Alobo. PCOS; Arguably the most comman endrocrinopathy associated with significant morbidity in women. The Journal of Clin. Endocrin. and Metabolism, 1999; 84: 1897-1899.
- 9. 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, 1995; 10: 2107-2111.
- 10. Evans D. J., Barth, J. H and Burke C. W. Body fat topography in women with androgen excess. International Journal of Obesity, 1988; 12: 157-162.
- 11. 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, 1935; 29: 181-191.
- 12. Pettigrew R and Hamilton Fairley D. Obesity and female reproductive function. British Medical Bullentin, 1997; 53: 341-58.
- 13. Mitchell. G. W and Rogers J. The influence of weight reduction on amenorrhoea in obese women. New England Journal of Medicine, 1953; 249: 635-7.
- 14. Futterweit W, Dunaif A, Veh C and Kingley P. The Perspective of hyperandrogenism in 109 conductive female patients with diffuse alopecia J. Med. Acod. Dermatol, 1988; 19-831-36. 40 Mishra and Sinha.
- 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, 2000; 85: 3496-3506.
- 16. 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.

- 17. Theresa L Max and Adv. E. Mehta: Polycystic ovary syndrome: Pathogenesis and treatment over the short and long term. Cleveland Clinic. Journal of Medicine, 2003; 70: 31-45.
- 18. Keri Marshall. Polycystic ovary syndrome; clinical consideration. Alter. Med. Rev, 2001; 6(3): 272-272.
- 19. Royal College of obstetrician and Gynecologist. Long term consequences of polycystic ovary syndrome. Guideline no 33; May, 2003; 1-8.
- 20. 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.
- 21. Jacobs DS, DeMott WR and Oxley DK. Luteinizing hormone, blood, and urine. Jacobs and DeMott laboratory test handbook, fifth edition, Hudson: Lexi-Comp Inc, 2001; 219-20.
- 22. Randall B Barnes, Adrienne B. Neithardt, and Suleena Kaha: Hyperandrogenism. Hirsulism and polycystric ovary syndrome. Chapter 6 in; Female reproductive endocrinology.
- 23. Gorakhnath chaturvedi, Charak Samhita, vidhotani, hindi teeka, Published by Chowkhamba bharti akadami, Varanasi reprint, 2012; 845.
- 24. Prof K. R. Srikantha murthy, Sushruta Samhita. English translation, volume 3rd, Published by Chaukhambha orientalia, Varanasi, reprint, 2017; 172.
- 25. Gorakhnath chaturvedi, Charak Samhita, vidhotani, hindi teeka, Published by Chowkhamba bharti akadami, Varanasi reprint, 2012; 845.
- 26. Prof K. R. Srikantha murthy, Sushruta Samhita. English translation, volume 3rd, Published by Chaukhambha orientalia, Varanasi, reprint, 2017; 171.
- 27. Prof. P. V tiwari, Kashyap Samhita. English translation, Published by- Chaukhambha visvabharti, oriental publishers and distributors. Varanasi, reprint, 2018; 357.
- 28. Prof. P. V tiwari, Kashyap Samhita. English translation, Published by- Chaukhambha visvabharti, oriental publishers and distributors. Varanasi, reprint, 2018; 357.
- 29. Stein I. F and Levanthal M. L. Amenorrhoea associated with bilateral polycystic ovaries. American Journal of Obstetrics and Gynecology, 1935; 29: 181-191.
- 30. 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 hypreandogenism. Human Research, 1993; 39: 179-187.

- 31. Marilyn R Richardson. Current perspective in PCOS. Am. Fam. Physician, 2003; 68: 697-704.
- 32. Acharya Yadav ji Trikam ji, Charak Samhita, Ayurved Dipika, Published by Chaukhamba Orientalia, Varanasi, Reprint, 2015; 187.
- 33. Prof. Siddhi Nandan Mishra, Ras Ratna Sammucchay, Hindi Commentary, Published by –Chaukhamba Orientalia, Varanasi, Reprint, 2017; 120.
- 34. Shri Sadanand Sharma, Ras Tarangini, Published by Motilal Banarasi Das Delhi, Reprint, 2009; 604.
- 35. Prof. Siddhi Nandan Mishra, Rasendra Choodamani, Hindi Commentary, Published by Chaukhamba Orientalia, Varanasi, Reprint, 2017; 247.
- 36. Prof. Siddhi Nandan Mishra, Ras Ratna Sammucchay, Hindi Commentary, Published by –Chaukhamba Orientalia, Varanasi, Reprint, 2017; 30.
- 37. Prof. P. V tiwari, Kashyap Samhita. English translation, Published by- Chaukhambha visvabharti, oriental publishers and distributors. Varanasi, reprint, 2018; 264.
- 38. Gorakhnath chaturvedi, Charak Samhita, vidhotani, hindi teeka, Published by Chowkhamba bharti akadami, Varanasi reprint, 2012; 1107.