

STUDY THE OVERVIEW OF RECENT MANAGEMENT OPTIONS FOR POLYCYSTIC OVARIAN DISEASE

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ABSTRACT: Infertility, though not a physically debilitating disease, severely affects the couples' psychological, harmony, sexual life and social functions. With all the modern needs of contraception rising on one side, infertility is still a major challenge to the gynecology practitioners on the other hand.

Male & Female contribute to the fertility of a couple and factors affecting any of reproductive organs can alter the fertile potential. Of all the factors contributing to female infertility due to ovarian disturbances, Polycystic Ovarian disease is the leading one.

PCOS is the commonest endocrine disease in women of reproductive age. It affects 5-10 % of women of reproductive age.¹ It is associated with increased androgen secretion, hirsutism, menstrual irregularities and infertility. It has impact not only on physical but also on mental health of women. PCOS now proves to be a significant factor in female infertility with prevalence of 0.6 to 3.4 % in infertile couples. It is noted in 30-50% of women with RPL (recurrent pregnancy loss).² With improving laboratory facilities, sonography and with routine laparoscopic evaluation of infertility. PCOD has shown a remarkable increase of incidence in recent years.

The aims of this study are 1. To know the patho-physiology of PCOS & its clinical correlation 2. To evaluate investigations 3. To compare recent modality of management options & their outcome.

KEY WORDS: PCOS-INFERTILITY-MENSTRUAL IRREGULARITY

INTRODUCTION: Polycystic Ovarian disease was described as early as 19th century. In 1935 Stein & Leventhal described syndrome of amenorrhea associated with polycystic ovaries.³

PCOS is the commonest endocrine disease in women of reproductive age. It affects 5-10 % of women of reproductive age. PCOS now proves to be a significant factor in female infertility. As women with PCOS are at increased risk of diabetes, hypertension, cardiovascular disease, hyperestrogen related cancers; it requires thorough evaluation & treatment. With growing experience since the beginning of 21st century various modalities with varying results have come into existence for its management.

Weight loss and dietary changes appears to affect all parameters of hormonal fluctuation. For menstrual irregularities, O.C.Pills is excellent choice of drug. Cyclic Progestin may be alternative. Antiandrogens are effective for excess hair growth. To trigger ovulation, Medical management with ovulation inducing drugs like Clomiphene Citrate is the first choice of

treatment for anovulation. Metformin most widely used insulin sensitizer for ovulation induction in patients with insulin resistance. Surgical Management with reduction of androgen production improves ovarian response to gonadotropins.

AIMS AND OBJECTIVES

- 1) To study pathophysiology of PCOS & its clinical correlation.
- 2) To evaluate different investigations for PCOS.
- 3) To establish different diagnostic criteria.
- 4) To compare recent modality of management options & their outcome
- 5) Long term follow up reduce consequence

Diagnostic Criteria for PCOS

Major:

- 1) Chronic Anovulation
- 2) Hyperandrogenemia
- 3) Clinical Signs of Hyperandrogenism

Minor:

- 4) Elevated LH: FSH ratio
- 5) Insulin Resistance
- 6) Perimenarchal onset of Hirsutism & Obesity
- 7) Intermittent anovulation associated with hyperandrogenemia

INVESTIGATIONS:

Ultrasonography: on TVS

- Thickness of tunica albuginea
- Hyperthecosis
- Multiple subcapsular cysts of 5-8 mm diameter
- Increased volume of ovary L X W X T X 0.523

On basis of USG, two type of PCO pattern have been identified¹⁹:

- 1) Peripheral cystic pattern
Small cysts are located in the subcapsular region and arranged in a "NECKLACE" or "STRIN OF PEARL" pattern.
- 2) General cystic pattern
Small cysts of variable size occupy both subscapular region and stromal part of ovary
Increased endometrial thickness due to unopposed estrogen stimulation in PCOS patients.

Color Doppler & 3D Scan in PCO:

Laboratory Investigation for Hormonal Evaluation:

- 1) Gonadotropins: S. LH, S. FSH level should be done on day 2 of cycle.
- 2) Androgens: S. Testosterone: Increased S. DHEA & Androstenedione: Increased SHBG; Decreased
- 3) Estrogens:
Total E2: Normal
Free / Unbound E2: Elevated due to decreased SHBG Serum estrone E1 ; Increased
- 4) Prolactin: Increased

5) Others:

S. TSH to rule out thyroid disorders.

Test for insulin resistance like S. insulin, fasting glucose, and fasting glucose: INSULIN RATIO, 2 HR gtt ETC.

Laparoscopy: Diagnostic and therapeutic purpose.

TREATMENT

- 1) Treatment of Menstrual Irregularities: O.C. Pills are drug of choice and combination of ethinyl estradiol and Metformin.
- 2) Treatment of Obesity: Weight reduction
- 3) Treatment of Hirsutism: Hormonal Therapy: OC Pills, Medroxy Progesterone, GnRH analogues, Glucocorticoids Antiandrogens: Spironolactones, Cyproterone Acetate, Flutamide Enzyme Inhibitors: Ketoconazole ,Finasteride Mechanical Method: Depilatory creams, Electrolysis, Laser hair removal, Waxing, Shaving , Bleaching etc.
- 4) Treatment of Infertility: Ovulation Induction can be achieved medically or surgically.

Clomiphene citrate: first line of drug is a weak synthetic estrogen but it mimics the action of an estrogen antagonist when used for ovulation induction in case of PCOS, starting dose should be 50 mg/day on day 2 to day 6 after onset of menses. Ovulation should be documented using TVS. Inj. HCG 10000 IU can be used for follicular rupture and followed by planned relations or IUI.

Results: Ovulation rate -80-85 %

Pregnancy rate - 40-45 %

Side Effects: Nausea, Breast pain, Pelvic discomfort, vasomotor flushes, Multiple Pregnancy.

Metformin: It is the most widely used insulin sensitizer for ovulation induction.

500 mg once a day breakfast x 4 days

500 mg twice a day with breakfast & dinner x 4days

500 mg with breakfast & 1000 mg twice a day. Thereafter up to 1000 mg twice a day.

Result: Ovulation rate 70%

Pregnancy rate 30 %

Gonadotropins: Various injectable preparations of HMG containing equal amount of FSH (75 IU) and LH (75IU) or highly purified FSH derived from recombinant DNA technology can be used. This treatment requires daily injection and close monitoring using TVS and S. estradiol.

Letrozole: It is aromatase inhibitors. Aromatase is an enzyme that converts androgen to estrogen.

Surgical Management:

Ovarian Wedge Resection

Laparoscopic Electrocauterisation of Ovarian Surface (LEOS)/ Laparoscopic Ovarian Drilling.

Treatment of Associated Factors:

Treatment of hypothyroidism

Treatment of oligospermia

Bromocriptine for hyperprolactinemia etc.

Materials and Methods

Present study is based on 100 patients of proved polycystic ovarian syndrome with chief complaints of menstrual irregularity and infertility. Suspected cases of PCOD sent for USG and special investigations.

Polycystic Ovarian Syndrome was proved by

- Clinical Signs and symptoms
- TVS
- Laparoscopy
- Laboratory Investigations

Summary and Conclusion: 100 cases of proved PCOD patients are studied with chief complaints of infertility and menstrual irregularities.

Majority of patients belong to 20-30 years of age group. Mean age of patients is 25 years suggesting it to be the disease of younger patients. Majority of patients came with complaints of infertility, menstrual irregularity(41%), Hirsutism (15%), Obesity (20%).

Ultrasonography (TVS) showed changes of PCOD in 82% while in remaining cases the ovaries appeared normal suggesting that anatomical variation is not the pathophysiology mechanism behind the disease.

All patients in this study were treated with a view to achieve fertility.

- a) Clomiphene Citrate: Ovulation rate 50% and conception rate 20%
- b) Metformin: Ovulation rate 70% and conception rate 23.3%
- c) Laparoscopic Ovarian Drilling: Ovulation rate 80% and conception rate 65%.

CONCLUSION: Polycystic ovarian syndrome is common endocrinopathy seen in women of reproductive age. However, confusion still exists over precise etiology. Interestingly PCOS is associated with wide spectrum of diverse clinical features. Role of insulin resistance, hyperandrogenism and a genetic predisposition have enhanced our understanding of conception.

Advances in technology have improved our efforts towards an accurate diagnosis. Multiple beneficial therapeutic options are available & have to be individualized in the management of PCOS patients. PCOS has significant long term metabolic impact on multiple organ systems and thus requires thorough evaluation to improve the quality of life of these.

BIBLIOGRAPHY

1. Asbjorn Aakavaag, Halvard Gjonnaess British Jrnl of Obst. 7 Gyn. Vol. 92, 1985.
2. Barbieri RL. Am Jrnl of Obst.Gyn. 2003.
3. Calvo RM et al; role of Follistatin gene in women with PCOS.
4. Clark AM, Thornley B., Tomlinson et al Hum. Repro. 1998, 13; 1502-1505.
5. Dewaart MJ et al infertility 1987: 10: 33-39.
6. Dickey et al, Hum Repro 1997.
7. Dunaif, A. 1997 Endo. Review 18; 774-800.
8. Farquhar, C., Vandekerckhove, P., Arnot, M. & Lilford R. 2001.
9. Felemban A, Tan SL, Tulandi T., Fertil Steril 2000, 73; 266-269.
10. Fox et al, 1991, Robinson 1992.
11. Fox R., Aust NSJ Obst. Gynaecol 1999; 39; 63-68.
12. Franks Gharani N., Waterworth D et al Hum. Repro. 12, 1997: 2641-48.

13. Franks, J., Adams, H. and Mason D. 1995 clinical obstet Gynaecol 12: 603-633.
14. Glueck et al, J. Phillips, H. Cammeron, D. Sieve – smith L., Wang P. 2001-2002.
15. Glueck et all 2001 Coetzee & Jackson 1984, 85 Heard et al 2002.
16. Greenblatte 7 Casper R American J Obst. & Gyn. Vol. 92, 1985
17. Hisao Sumioki, Michio korenaga fertility & Sterility Vol. 50 No.4 1988.
18. James F. Daniell, Wayne Miller Fertility & Sterility Vol. 51 No. 2 1989.
19. Kolodziejczyk B et al Feril Steril 2000, 73 ; 1149-1154.
20. Mitwally MF, Casper RF, Fertil Steril 2001; 75: 305-309.
21. Naether OGJ et al Fertil Steril 1993; 60: 95-98.
22. Nestler J., Stovall D., Akhter S., Luorno M., & Jakubowicz D 2002.
23. Nestler R., Powers, L., Matt, W., Steingold K., Plymate R., Rittjmaster S. 1991.
24. Nestler, J., Jakubowicz, J., Lurono, J., 2000 J Pediatr., Endocrinol. Metab.S: 1295-1298.
25. Neveu N, Granger L, St. Michel P lavoie Fertil Steril 2007, 87, 113-120.
26. Norman, J., Davies, J., and Moran J., 2002. J. Endocrinol Metab, 13: 251-257.
27. Rosenfied RL, Barnes, RB., Cara JF. & luckey. A.W. Fertility & Sterility 53, 1990, 7785- 91.
28. Rotterdam ESHRE/ ASRM PCOS consensus workshop revised 2003, Fertil Steril 2003, 81; 19-25.
29. Seli, E. and Duleba J. 2002. Hum. Repro. 17, 2230-2236.
30. Speroff, L. Glass R & Kase G. 1999 clinical Gyn, Endo. & Infertility 6th edition 487-521.
31. Stadtmauer LA, Toma K, Rient M & Tablert M 2001 Fertil Steril 2001; 75, 505-509.
32. Stadtmauer, A., laurel, C., & Sergio 2002 Hum. Repro, 17, 3016-3025.
33. Stein et al, Am Jrnl of Obst. Gynecol 1948.
34. Stein IF and Leventhal ML. 1935 American Jrnl of Obst. & Gyn., 58, 181-191.
35. Yen et al, J of clin endocrine & Metab 1970.
36. Yen, 1980; lobo et all 1981 Shoupe, kumar & lobo 1983.

OBSERVATION AND DISCUSSION

Table: 1: Age Distribution of PCOD Cases:

Age of Patients (Years)	Total no. of cases	Percentage
Less than 20	06	6%
Between 21-25	58	58%
Between 26-30	34	34%
More than 30	02	02%

Table: 2: Frequency of complaints:

Chief complaints	Total no. of cases	Percentage
Infertility	100	100%
Menstrual Irregularities	41	41%
Hirsuitism	15	15%
Obesity	20	20%

All patients studied basically came with complaints of infertility followed by menstrual irregularities.

Table: 3: Types of Infertility

Type of infertility	Total no. of cases	Percentage
Primary	60	60%
Secondary	40	40%

ORIGINAL ARTICLE

Table: 4: Value of Luteinizing Hormone(LH)

Luteinizing Hormone	Total no. cases	Percentage
Elevated	85	85%
Normal	15	15%

Normal LH Value in follicular phase 5-20 mIU/ML.

Table: 5: Follicular Stimulating Hormone (FSH)

FSH	Total no. cases	Percentage
Normal	94	94%
Below Normal	06	06%

Normal FSH Value in follicular phase 4.5-20 mIU/ML.

Table: 6: LH: FSH Ratio:

LH: FSH Ratio	Total no. of cases	Percentage
1-1.5	12	12%
1.6-2	32	32%
>2	55	55%

Normal LH:FSH ratio is around 1 in early follicular phase.

Table: 7: Success Rates with Different Regimens:

Modality of Treatment	Total no. cases	Ovulatory Rate	Conception Rate	Abortion Rate
Clomiphene Citrate	30	50%	20%	33.3%
Metformin	30	70%	23.3%	14%
Laparoscopic Ovarian Drilling	40	80%	65%	19.23%

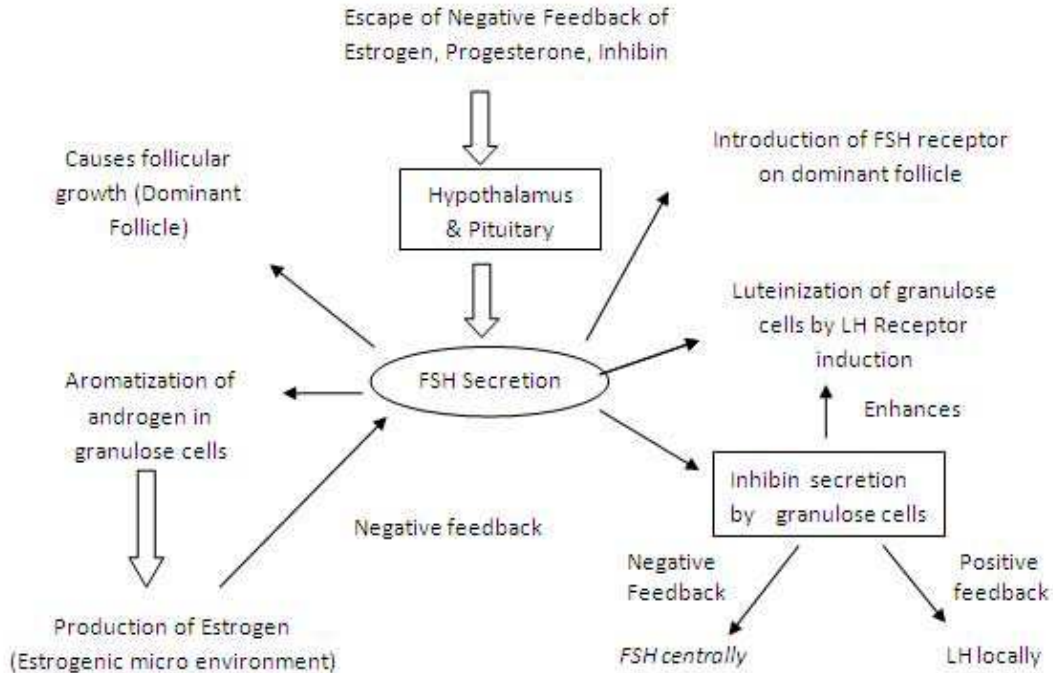
Table: 8: Overall Results of Treatment:

	Treatment Given	Ovulatory Rate	Conception Rate	Live birth	Abortion Rate
Total no. cases	100	68	39	31	8
Percentage	100%	68%	39%	79.49%	20.51%

PATHOPHYSIOLOGY OF PCOS

Normal events in the ovary leading to ovulation:

- A. Sufficient FSH stimulation for initial follicular recruitment and growth of dominant follicle.

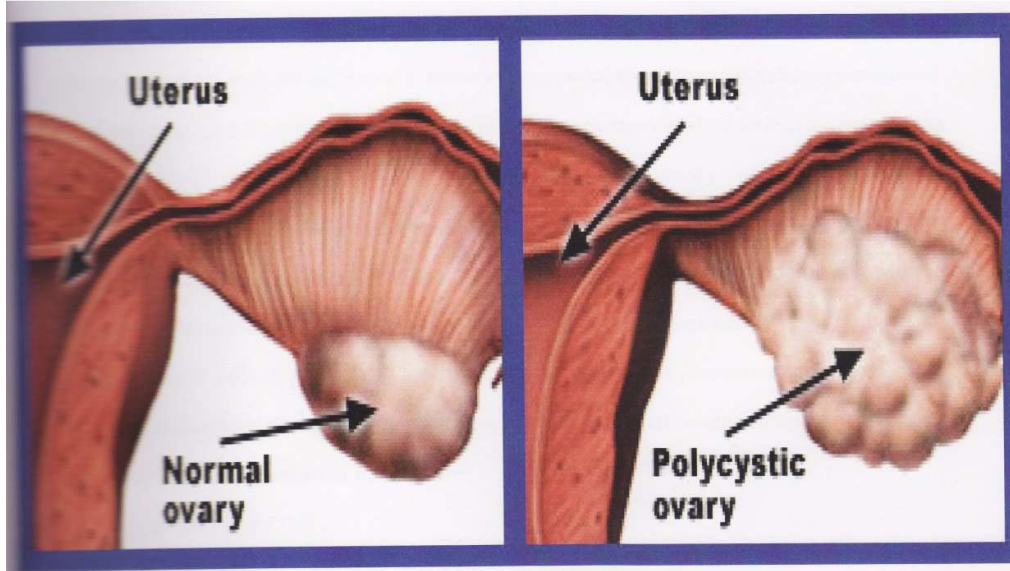


PCOS & Obesity: 35-60 %, usually android type. BMI > 27 KG/ SQ. M. ; Waist hip ratio > 0.85 & Waist >100cm usually associated with hyperinsulinemia.

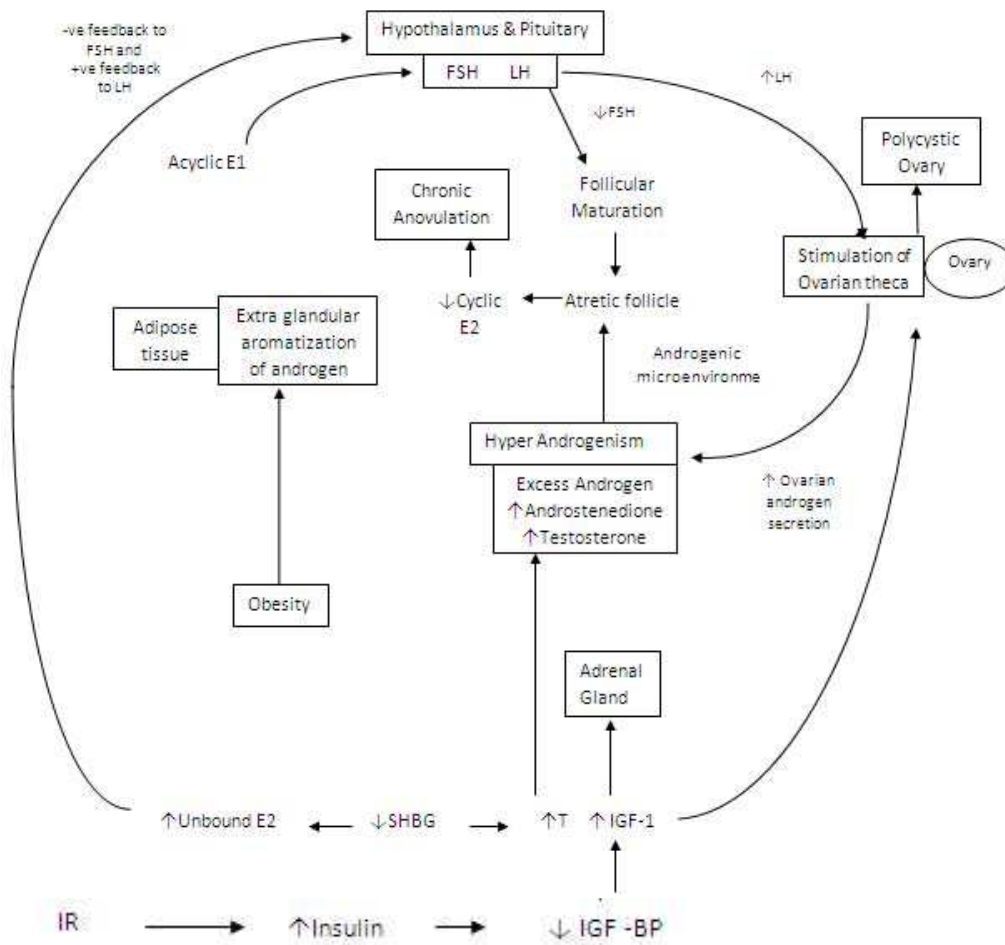
Hyperandrogenism with chronic Anovulation: 50-60 %

Hyperinsulinemia and PCOS Insulin Resistance,: Causes

- Peripheral Target tissue resistance
- Decreased Insulin Receptor Number
- Decreased Insulin Receptor Binding
- Post Receptor Failure most important
- Decreased Hepatic Clearance
- increased Pancreatic Sensitivity



PCOS AT GLANCE



Symptomatology and Clinical Features

1. Infertility
 2. Menstrual Irregularities
 3. Hirsutism
 4. Obesity
 5. Depression And Anxiety
- Long Term Consequence of PCOS:

