RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

A Cross Sectional Study of Clinical Profile, Biochemical & Hormonal Studies of Polycystic Ovarian Disease .

KEYWORDS: PCOD (Polycystic ovarian Disease),Hyperinsulinemia,BMI (Body Mass Index), LH/FSH-Luteinizing hormone & Follicle stimulating hormone ratio, HOMA index-Homeostatic model assessment.DM(Diabetes Mellitus).

Dr. Jayshree Awalekar.	Dr. Chidanand Awalekar.	Dr. M. H. Patwardhan
M.D. Professor, Dept of Medicine Bharati Vidyapeeth Deemed University Medical college & Hospital, Sangli.	M.D. Professor &Head Of Dept, Medicine Bharati Vidyapeeth Deemed University Medical college & Hospital, Sangli.	M.D.D.M.(Endocrinology Patwardhan Endocrinology & Research centre,Miraj

ABSTRACT *Polycystic ovarian disease (PCOD) is a common endocrine disorder. Clinical, Hormonal & biochemical profile was studied in PCOD cases. Majority of young females are affected. Insulin resistance is main causative factor for all these consequences & morbidity. Along with hyperinsulinemia, dysfunction of hypothalamopituitoryadrenal axis is a key etiological factor in development of all manifestations of PCOD & cause hyperandrogenism(4,5). They present with Irregular menses, Infertility, Obesity, Hirsutism, Acanthosis Nigricans etc.Investigations done are LH (Luteinizing Hormone), FSH (Follicle stimulating hormone) & Serum Insulin levels. Hormonal derangement & hirsutism was studied by LH/FSH Ratio, Resistance to insulin is diagnosed by HOMA-IR levels ≥6.8(26).Our study shows irregular menses in 62 % of PCOD cases, Hirsutism in 34%,Infertility in 40% cases ,Acanthosis Nigricans in 86% of PCOD cases & acne in. 23%.Following manifestations of PCOD are also documented in our study. Diabetes Mellitus - 19% Hypertension in 4%, Cardiac disease-1%.Following observations were noted- BMI->25 observed in 65 %patients, Waist/Hip Ratio- >0.8 is observed in 30%,HOMA Index was increases in 82% of PCOD cases.*

Introduction-

Polycystic ovarian disease (PCOD) is a common endocrine disorder. It is also known as Stein Leventhal syndrome. Polycystic ovary syndrome is a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan"[5] The symptoms of PCOS vary with age, race, weight[2],. Majority of young females of reproductive age are affected. Insulin resistance along with dysfunction of hypothalamopituitoryadrenal axis causing androgen excess is a key etiological factor in development of all manifestations of PCOD[5,9]. It presents with irregular menses, infertility, obesity, Hirsutism.

The exact prevalence of PCOS is not known due to varied definitions. Globally, prevalence of PCOS are highly variable, ranging from 2.2% to as high as 26%[2,11].The prevalence in Indian women of reproductive age is 5-10%.According to Rotterdam-2003criteria, the prevalence among the general female population will raise up to 10%.[3] Nidhi, *et al* have reported a prevalence of PCOS in 9.13% of the Indian adolescents[15].

National Institutes of Health (NIH) consensus conference 1990, PCOS was defined as chronic anovulation with clinical and/or biochemical hyperandrogenism, with exclusion of other mimicking aetiologies, such as thyroid or adrenal dysfunction( ).

In 2003 a consensus workshop sponsored by ESHRE/ASRM in Rotterdam indicated PCOS to be present if any 2 out of 3 criteria are met .[2,7,8] It also includes many women without androgen excess. Rotterdam criteria[2] has been adopted world over.

1. oligoovulation and/or anovulation.
2. Excess androgen activity.
3. polycystic ovaries (by gynecologic ultrasound)- Ovaries are larger than normal and have multiple small ovarian cysts.

Polycystic ovaries are not necessarily associated with USG evidence of polycystic ovaries. The prevalence of polycystic ovary syndrome varies widely according to the definition applied [1].

4. Infertility.

Other entities are excluded that would cause these.[5,8]

However, recently in 2006, Androgen Excess Society (AES) has come up with a consensus statement, defining PCOS as a hyperandrogenic state and emphasises the presence of either clinical and/or biochemical features of hyperandrogenism along with other features of PCOS for diagnosis.[2]

Insulin resistance(IR)- is main causative factor for all these consequences & morbidity. Failure of the target cells to respond to normal or ordinary levels of insulin is regarded as insulin resistance regardless of the body mass index (BMI). Hyperinsulinaemia due to insulin resistance occurs in approximately 80% of women with PCOS and central obesity. In 30%–40% of lean women diagnosed with PCOS [4,5]. we have used HOMA index as a marker of insulin resistance, based on measurements of fasting glucose and insulin levels, is the homeostatic model assessment (HOMA-IR). Resistance to insulin is diagnosed at HOMA-IR levels ≥3 [26].

Insulin resistance can manifest as follows:

1. Obesity[1,3,14]
2. Type II diabetes [1,4].
3. Infertility-
4. Hirsutism-
5. Acanthosis nigricans- (patches of darkened skin under the arms, in the groin area, on the back of the neck [15]
6. Cardiovascular disease- two fold increased risk of arterial disease in PCOS patients as compared to women

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

without PCOS [7,14].
7. Hypertension , in obese and/or during pregnancy [1]
8. Strokes [2,3]
9. Weight gain
10. Abortion [6,7,]
11. Sleep apnoea, in obese[7,14]
12.Non-alcoholic fatty liver disease, in obese [14,15]

Obesity- Obesity is defined as an excessive accumulation of in the body resulting in adverse effects on health of the individual[17]I. It can be measured by BMI(Body Mass Index) and /or waist-to-hip circumference ratio (WHR). > 0.8 is normal.

BMI -It is calculated as Height in Metre^2/weight in Kg. The currently recommended cut-offs of BMI recommended by World Health Organization include[17], It is as follows-

	BMI
Normal	18.5-24.9
Overweight	25.0 - 29.9
Obesity	>30 kg/m2 for obesity.

Irregular Menses- Menstrual irregularity is a common feature of PCOS, occurs in more than 75% of the adult PCOS population [10,14]and is often the earliest clinical manifestation in the adolescent[.15] It is defined as menses that occur at intervals of greater than 6 to 8 weeks in the absence of thyroid, adrenal, or other pituitary dysfunction. But it is not be the sole criterion for PCOS. It comprises an important symptom that should be followed in the adolescent. When oligomenorrhea is persistent or presents in conjunction with symptoms of androgen excess, possibility of PCOS needs to be ruled out.

Infertility - The annual incidence of infertility due to PCOD per million was 41 with overt PCOD and 139 with occult PCOD of total 180.[10,18]Insulin resistance or hyperinsulinemia cause abnormal functioning of hypothalamic-pituitary-ovarian axis that lead to PCOS.They have increased frequency of hypothalamic GnRH pulses, androgen excess . Increased androgen levels, primarily produced by the ovaries (with a smaller contribution from the adrenals and peripheral adipose tissue) interfere with hypothalamic sensitivity to negative feedback from the ovary, thereby increasing GnRH pulse frequency[10,.7] This persistently rapid pulse frequency favours increased LH secretion,8 which in turn stimulates the ovarian theca cells to produce more androgens. The relative decrease in FSH secretion leads to less aromatization of androgens to estradiol and impaired follicular development, resulting in the prolonged periods of oligomenorrhea that are characteristic of PCOS. which in turn results in an increase in the LH/FSH ratio[8,22]. Normally it is 1:1,may increase upto 3:1.More than 3 is supposed to be altered.

Hirsutism- Adipose tissue enzyme, aromatase, converts androstenedione to estrone and testosterone to estradiol. The excess of adipose tissue in obese have excess androgens, which are responsible for hirsutism and virilization Excess estrogens inhibits FSH via negative feedback. Thus reduce FSH levels & contributes in alteration of LH/FSH ratio. [15] Both insulin resistance and hyperinsulinemia are more severe in adolescents with PCOS compared with the general adolescent population.11 Insulin stimulates ovarian theca cell synthesis of androgens12 and inhibits hepatic production of sex hormone-binding globulin[10.13] Together, these effects result in increased circulating free androgen levels, thus perpetuating the underlying pathophysiology of PCOS.

Clinical symptoms of **androgen excess** are severe acne or hirsutism, suggest immediate evaluation for PCOSeven reliability of these clinical symptoms of hyperandrogenism is low. Increased serum androgen levels provide the best measure of androgen excess in the adolescents[12,14].

High Blood Pressure- clinical manifestations of PCOS are heterogeneous, the hallmarks of the syndrome remain anovulation, androgen excess, and insulin resistance. Each of these features of the syndrome is responsible for the promotion of hypertension in this population. Therefore, therapy for hypertension should be targeted at treatment of these underlying abnormalities[18].

Cardiovascular Diseases- women with PCOS manifest several cardiovascular disease risk factors.One study employed menstrual irregularity as a proxy for PCOS in a prospective cohort study of 82,439 female nurses ages 20-35 years old.[10] During a fourteen-year follow-up, women with "usually irregular" or "very irregular" menstrual cycles had an increased risk for nonfatal or fatal coronary heart disease compared to women with "very regular" menstrual cycles[19].

At long-term follow-up, a history of nonfatal cerebrovascular disease and cardiovascular risk factors including diabetes are more prevalent among women with polycystic ovary syndrome. Morbidity and mortality from of coronary heart disease among women with polycystic ovary syndrome is not as high as previously predicted.On the contrary less supporting data is available in this regard[19,25].

Diabetes Mellitus- PCOS was associated with a unique disorder of insulin action, as well as defects in insulin secretion, and together these abnormalities conferred a substantially increased risk of glucose intolerance. Further they can develop Diabetes. In addition to insulin resistance, beta cell dysfunction is present in PCOS and it is the combination of these two derangements that contributes to the development of T2DM.(10,23) The beta cell dysfunction seen in women with PCOS has been evidenced by several methods demonstrating impaired insulin secretion response to glucose and exists independently of impairment in glucose tolerance. Notably, the impaired insulin secretory response was observed most convincingly among the women who had first degree family members with T2DM. [19]

This can help in solving many problems where etiology is PCOS rather than looking at only obesity,Diabetes,Ischaemic Heart Disease,Infertility as a single.

Material & Methods-
Study Design, Size & Duration-
Cross sectional study ,This was a carried out at Department of Medicine & Obstetrics & Gynaecology at Bharati Vidyapeeth Deemed University & Medical College Hospital, Sangli (Tertiary Care Centre) & Dr.Patwardhan's Endocrinology Clinic & Research Centre, Miraj.

It was carried out from Januray 2013 to January 2015.

101 cases of PCOD diagnosed by using Rotterdam criteria are included in this study.

A. Written consent is taken before starting examination.
B. Clearence from ethical committee is taken.

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

History & Clinical examination is done.
1. Age Group-
2. Body Mass Index (BMI)-
3. Menstrual irregularities-amenorrhoea, oligomennorrhoea & irregular cycles are included in this group.
4. Infertility
5. Hirsutism-unwanted hair growth, acanthosis nigricans.

B. Following investigations were done-
1. LH (Luteinizing Hormone).
2. FSH (Follicle stimulating hormone).
3. Serum. Prolactin levels-
4. Serum Insulin levels-

C.
1. BMI-
2. LH/FSH Ratio- The ratio of LH (Luteinizing hormone) to FSH (Follicle-stimulating hormone), when measured in international units, is elevated in women with PCOS. Common cut-offs to designate abnormally high LH/FSH ratios are **2:1**or **3:1** as tested on Day 3 of the menstrual cycle [22].
3. HOMA Index- HOMA Index-homeostatic model assessment (HOMA) -method used to quantify IR & beta-cell function.It also predicts cardiometabolic risk .Calcualated by using formula HOMA-IR = [Glucose] x [Insulin] / 405 (Glucose in mg/dl)[12].

Results-
1.Age group-15-35 yrs.
1. BMI->25 observed in 65 %patients.
2. Waist/Hip Ratio- >.8 is observed in 30%.
3. DM- 19%
4. HTN - 4%
5. Cardiac disease-1%
6. Hirsutism-
7. Acanthosis Nigricans-
8. Acne-

Calculations- done by using Microsoft Exel .

Results-
Graph showing % clinical features of PCOD in our study group

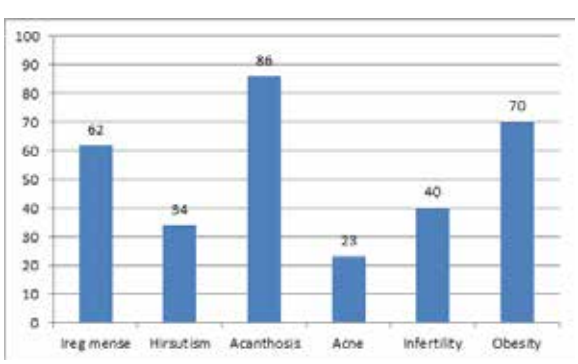

Table.1 showing variables & its observations.

Variable	Normal values	N	Mean	Minimum	Maximum	Std Dev
BMI	<25	101	27.21	13.9	31.9	--
LH/FSH	<3.8	101	2.35	0.19	9.91	1.35
Age	- Normal	101	21.70	15	35	4.17
S. Insulin	3-17	101	87.33	17.9	121	83.54
BSL-Fasting	<120mg%	101	100.17	53	192	24.09
HOMA Index	<6.8	101	21.15	3.18	121.74	18.29

In our study 70 % patients were obese of them 65% patient's BMI>25 & W/H ratio >.8 was observed in 69 %.

LH/FSH ratio was increased if it is >3.8, minimum 0.19, was maximum was 9.91 & Mean was 2.35

HOMA index was increases if it is >6.8 It was increased in 72 %

S. Insulin levels were minimum 17.9 ,maximum & Mean-87.33 was above Normal.

Diabetes Mellitus-19% patients had high blood sugar levels, needed antidiabetic treatment along with PCOS treatment.

Hypertension-4% of PCOD patients had hypertension. Of these1 had acute myocardial infarction,needed angioplasty.

Hirsutism-34% had signs of hirsutism, hair loss.

Acne-23% cases had acne.

S. Testesterone was mildly increased in 30% cases. Increased serum androgen levels provide the best measure of androgen excess in the adolescents.

Discussion-
Obesity in women with polycystic ovary syndrome is prevalent in North America. In an unselected population from Alabama, 24% of women with the syndrome were overweight (body mass index [BMI] 25·0–29·9) and 42% were obese (BMI >30).

10 In a study from the Netherlands, the mean BMI was 28–29, and prevalence studies have shown BMIs in the range of 25–28 in the UK, Greece, and Finland.11 prevalence of excessive weight in women with polycystic ovary syndrome in the USA is high.

DA Rodin et al. There were significant associations between PCO and menstrual irregularity; infertility; the presence of acanthosis nigricans and the fasting blood glucose concentration.

There were many clinically signs & symptoms contributing PCOS. Although IR is a common abnormality in PCOS. In PCOS women, the prevalence of IR was 64% according to the HOMA-IR measurement. Insulin resistance was observed in 26% patients according to HOMA-IR, and in 16% or 28% according to G0 /I0 or G120/I120, respectively. Obesity in 50%..Hyperinsulinemia is present in 50% PCOS.

The population studies revealed, first, that overt and occult PCOD accounted for 90% of patients with oligomenorrhea and 37% with amenorrhea, or 73% with oligo- or amenorrhea. Oligo- or amenorrhea accounted for 21% of couples with infertility .All patients presented either oligomenorrhea (31%), periods of secondary amenorrhea (9%), or both alterations (60%). The majority of the patients were infertile (75.6 percent). The LH/FSH ratio was higher than 2:1 in 55 percent of the patients and higher than 3:1 in 26.2 percent. The ultrasonographic aspect of the ovaries was considered to be normal in 31 percent.

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

Michelmore et al[21]. In this study they have shown PCOD was identified in 74 (33%, 95% CI = 27-39%) of the 224 women who underwent USG screening.Irregular menstrual cycles were 20% more common in women with polycystic ovaries than in women with normal ovaries (P = 0.07). There were no significant differences in acne, hirsutism, body mass index or body fat percentage between women with polycystic and normal ovaries. Analysis of biochemical data showed that women with polycystic ovaries had higher total serum testosterone concentrations (P = 0.03). The prevalence of PCOS in this age group was as low as 8% or as high as 26% depending on which criteria were applied to define the syndrome. PCOS women revealed greater mean BMI and lower fasting insulin concentrations and greater insulin sensitivity in polycystic ovary and PCOS groups when compared to women with normal ovaries.[1]

CONCLUSIONS:

The large spectrum of clinical manifestations in PCOS, probably due to insulin resistance-hyperinsulinemia & hyperandrogenism The main clinical feature of the PCO is the irregularity of menses,obesity,infertility,hirsutism and that the laboratory tests are important to diagnose PCOS.As its prevalence is increasing,needs suspicion of PCOs & diagnosis.This can help in solving many problems where etiology is PCOS rather than looking at only obesity,Diabetes,Ischaemic Heart Disease,Infertility as a single disease.

REFERENCE

1. Polycystic ovaries and associated clinical and biochemical features in young women. ClinEndocrinolOxf 1999; 51: 779 2. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. FertilSteril. Feb 2009;91(2):456-88. [Medline]. 3. Stein I, Leventhal M. Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynecol. 1935;29:181. 4. PCOS Consensus Workshop Group. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. FertilSteril. Jan 2004;81(1):19-25. [Medline]. 5. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J ClinEndocrinolMetab. Nov 2006;91(11):4237-45. [Medline]. 6.Marcos Yorghi et al,Polycystic ovary syndrome: Clinical and laboratory evaluation, Sao Paulo Med. J. vol.114 no.4 São Paulo July/Aug. 1996 6. Vause TD, Cheung AP, Sierra S, Claman P, Graham J, Guillemin JA, et al. Ovulation induction in polycystic ovary syndrome. J ObstetGynaecol Can. May 2010;32(5):495-502. [Medline]. 7. Barber TM, McCarthy MI, Wass JA, Franks S. Obesity and polycystic ovary syndrome. ClinEndocrinol (Oxf). Aug 2006;65(2):137-45. [Medline]. 8. .Goodarzi MO, Korenman SG. The importance of insulin resistance inpolycystic ovary syndrome. FertilSteril 2003;80:255–58. 9. Royal College of Obstetricians and Gynaecologists. Long-term consequences of polycystic ovary syndrome. London, UK: Royal College of Obstetricians and Gynaecologists; 2007. Green-top guideline; no. 33. [Full Text]. 10. Diamanti-Kandarakis E, Kouli CR, Bergiele AT, et al. A survey of the polycystic ovary syndrome in the Greek island of Lesbos: hormonal and metabolic profile. J ClinEndocrinolMetab. Nov 1999;84(11):4006-11 11. Alemzadeh R, Kichler J, Calhoun M. Spectrum of metabolic dysfunction in relationship with hyperandrogenemia in obese adolescent girls with polycystic ovary syndrome. Eur J Endocrinol. Jun 2010;162(6):1093-9. [Medline]. 12. Rosenfield RL. Clinical practice. Hirsutism. N Engl J Med. Dec 15 2005;353(24):2578-88. [Medline]. 13. Koulouri O, Conway GS. Management of hirsutism. BMJ. Mar 27 2009;338:b847.