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Original Research Article

## Evaluation of patients with polycystic ovarian syndrome at a tertiary care center

Swapna Y.<sup>1</sup>, V. Srilakshmi<sup>2\*</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Deccan College of Medical Sciences, Hyderabad, Telangana, India

<sup>2</sup>Consultant, Area Hospital, Golkonda, Hyderabad, Telangana, India

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**\*Correspondence:**

Dr. V. Srilakshmi,

E-mail: giridhar.gollapalli@gmail.com

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### ABSTRACT

**Background:** It has been estimated that prevalence of PCOS ranges from 5-10% in reproductive females. Thus, it becomes most common endocrinopathy in this age group. Lack of ovulation and androgen over activity are key features of PCOS. The objective of this study was to patients with polycystic ovarian syndrome at a tertiary care center.

**Methods:** Present study was following up study with 200 cases of PCOS. Rotterdam criteria were used for the diagnosis of the PCOS. This criterion includes three things. First is woman having in last year <6 periods of menstruation. Second is testosterone value >0.6 ng/ml and third is each ovary having >12 follicles with increased size and volume. Those cases with hypothyroidism, adrenal tumors, congenital adrenal hyperplasia etc were excluded from the present study. Those on steroid therapy were also excluded. Detailed history and clinical examination were carried out for included cases as well as required investigations.

**Results:** Overall incidence of infertility was found as 27.9%. Out of these 200 cases, 44 (22%) had PCOS. Majority cases belonged to 20-24 years of age. Hirsutism was most common findings in clinical hyperandrogenism. Risk of insulin resistance syndrome was 4.79 times higher in obesity compared to not obese. Age, BMI, duration of infertility, ovarian volume, and menstrual pattern had effect on ovulation rate following laparoscopic ovarian drilling. Increasing duration of infertility and BMI had lower ovulation rate. Ovulation rate was highest when treated with clomiphene citrate alone than the combination therapy.

**Conclusions:** Women with obesity have more chances of having PCOS as seen from the present study.

**Keywords:** Hirsutism, Hyperandrogenism, Insulin resistance, Polycystic ovarian syndrome, Syndrome

### INTRODUCTION

It has been estimated that prevalence of PCOS ranges from 5-10% in reproductive females. Thus, it becomes most common endocrinopathy in this age group. Lack of ovulation and androgen over activity are key features of PCOS.

Whenever anovulation is there, there are disturbances of the menstruation, in the form of complete absence of menses or reduced degree of menses. In cases of

hyperandrogenism, there is growth of facial hairs; increased incidence of acne, loss of hairs in androgenic fashion, there is increased levels of the testosterone.<sup>1</sup>

Women with PCOS tend to be obese. They can also have insulin resistance. Insulin resistance can be seen in underweight women with PCOS. Not only testosterone is increased but also the luteinizing hormone levels are also increased. At the same time, there is decrease in the production of sex hormone-binding globulin (SHBG).<sup>2</sup>

One of the most consistent features of PCOS is polycystic nature of ovaries which can be detected by ultrasonography. But it has been said that even in women with apparent no PCOS, one fifth of them may have polycystic ovaries. It is not easy to detect PCOS. Hence Rotterdam gave the criteria that out of three, if any two are present, then the women can be labeled as having PCOS. First is woman having in last year <6 periods of menstruation. Second is testosterone value >0.6 ng/ml and third is each ovary having >12 follicles with increased size and volume.<sup>3</sup>

In women with PCOS, there is presence of the insulin resistance. This leads to the increased levels of insulin in the blood. This leads to "ovarian hyperandrogenism". This leads to various manifestations of PCOS as described before.<sup>4</sup>

Apple shape obesity is common feature of android obesity. Pear shape obesity is common feature of gynoid obesity. In women with PCOS, android obesity is commonly seen. Obesity leads to increased intensity of the resistance of the insulin. It is commonly found to be associated with infertility and other features.<sup>5</sup> In women with PCOS, there is resistance to the action of insulin. This coupled with hyperinsulinemia causes increase in the triglycerides, LDL, VLDL and a decrease in the HDL, increase in the blood pressure levels. Women with PCOS are at an increased risk of developing diabetes and other non-communicable diseases.<sup>6,7</sup> Present study was carried out to study the incidence of PCOS among the various causes of infertility and to establish the fact that the operative Triple Puncture Video Laparoscopy has a very important role to play in the management of PCOD and it has the additional advantage of offering therapeutic measures at the same sitting.

## METHODS

The Study design is Present study was following study with Sample size: 200 cases of PCOS. The Criteria used Rotterdam criteria were used for the diagnosis of the PCOS. This criterion includes three things. First is woman having in last year <6 periods of menstruation. Second is testosterone value >0.6 ng/ml and third is each ovary having >12 follicles with increased size and volume. The Study period was September 2011 to October 2012. The Settings was Department of Obstetrics and Gynecology, Deccan College of Medical Sciences, Hyderabad, Telangana, India.

### *Inclusion criteria*

- Patients fitting in Rotterdam criteria,
- Willing to participate.

### *Exclusion criteria*

- Patients with co-morbidities like adrenal tumors, hypothyroidism, OC pill use, use of

glucocorticoids, use of anti-androgen drugs, use of drugs for diabetes,

- Not willing to participate.

Data was recorded regarding history, examination; investigations in a pre-designed, pretested, semi structured study questionnaire designed for the present study after the cases gave their informed consent.

Height and weight were measured as per the standard guidelines and protocol. Body mass index was calculated based on height and weight. Waist and hip circumference were measured as per the standard guidelines and protocol. Waist hip ratio was calculated based on the waist and hip circumference.

Presence of symptoms pertaining to PCOS were asked and noted. Patients were asked to give the fasting blood samples in the morning on any day from second to fifth day of the menstrual cycle. Double anti body RIA method was used for the determination of the fasting insulin levels. Glucose oxidase method was used for the determination of the fasting glucose levels. Other investigation like levels of LH, FSH and TSH were carried out. Curvilinear transducer with frequency 3.5 megahertz was used in trans-abdominal ultrasonography.

### *Statistical analysis*

The data was entered in the master chart of the excel sheet and analyzed using proportions and appropriate statistical test was applied as and when required.

## RESULTS

Table 1 shows incidence of infertility and the variability in clinical phenotypes characterizing PCOS cases. The overall incidence of infertility was found out to be 27.9% in the present study. Out of these 3170 cases with infertility, 200 cases were included in the present study. Out of these 200 cases, 44 had PCOS i.e. 22%. 80 cases had oligo ovulation i.e. 40%. 18 cases had hyper androgenism i.e. 9%. 18 cases had PCOS plus chronic anovulation i.e. 9%. 14 cases had hyperandrogenism plus PCOS i.e. 7%. 10 cases had hyperandrogenism plus chronic anovulation i.e. 5%. 16 cases had hyperandrogenism plus chronic anovulation+PCOS i.e. 8%.

Table 2 shows demographic details of cases studied. Majority of the cases belonged to the age group of 20-24 years of age. This was followed by 25% of the cases who belonged to the age group of 25-29 years of age. This was followed by 21.5% of the cases who belonged to the age group of less than 19 years of age. Only 12.5% of the cases belonged to the age group of more than 30 years of age. 55% of the cases were found out to be overweight. 38% of the cases were found to have grade 1 obesity. Only 7% of the cases were found out to be having obesity grade 2.

Table 3 shows clinical Hyperandrogenism among the study subjects. 48 cases i.e. 24% of the cases were found to have acne. 130 cases i.e. 65% of the cases were found to be suffering from hirsutism. 12 cases i.e. 6% of the cases were found to be suffering from androgenic

alopecia. 10 cases i.e. 5% of the cases were found to have acanthosis nigricans. Thus, hirsutism was the most common findings in clinical hyperandrogenism among the study subjects in the present study.

**Table 1: Incidence of infertility and the variability in clinical phenotypes characterizing PCOS cases.**

Total gynec patients	Total patients with infertility	Incidence of infertility
11350	3170	27.9
Criteria	No. of patients (n=200)	%
PCOS	44	22
Oligo ovulation	80	40
Hyper androgenism	18	9
PCOS+Chronic anovulation	18	9
Hyperandrogenism+PCOS	14	7
Hyperandrogenism+Chronic anovulation	10	5
Hyperandrogenism+Chronic anovulation+PCOS	16	8

**Table 2: Demographic details of cases studied (n=200).**

Demographic characteristics	Number	%	
Age (years)	<19	43	21.5
	20-24	83	41
	25-29	50	25
	>30	25	12.5
Body mass index (kg/m <sup>2</sup> )	<29	110	55
	30-34	76	38
	>34	14	7
Menstrual cycles	Regular	84	42
	Oligomenorrhea	98	49
	Amenorrhea	18	9

**Table 3: Clinical Hyperandrogenism among the study subjects.**

Characteristics	No. of Patients (n=200)	%
Acne	48	24%
Hirsutism	130	65%
Androgenic Alopecia	12	6%
Acanthosis Nigricans	10	5%

Table 4 shows insulin resistance in non-obese & obese PCOS. It was found that the prevalence of insulin resistance syndrome was 70% among those who were obese compared to 32.5% of insulin resistance syndrome among those who were not obese. This difference in the insulin resistance syndrome among the obese cases and the non-obese cases was found out to be statistically significant. On calculation of the odds ratio, it was found that the risk of insulin resistance syndrome was 4.79 times higher in those with obesity compared to those who were not obese with 95% confidence interval of 2.62-8.75.

Table 5 shows ovulation rates in PCOS patients who underwent laparoscopic ovarian drilling (LOD). These 200 patients who were diagnosed by Rotterdam’s criteria as PCOS were further evaluated by diagnostic laparoscopy and underwent ovarian drilling at the same sitting. They were followed up in the outpatient clinic for ovulation by TVS. It was found that age, BMI, duration of infertility, ovarian volume, and menstrual pattern had effect on ovulation rate following laparoscopic ovarian drilling. It was also found that increasing duration of infertility and BMI had lower ovulation rate.

**Table 4: Insulin resistance in non-obese and obese PCOS.**

Obesity	Insulin resistance present		Insulin resistance absent		Yate’s corrected chi square	p value	Odds Ratio	95% confidence interval
	Number	%	Number	%				
Yes	63	70	27	30	26.04	<0.0001	4.79	2.62-8.75
No	36	32.5	74	67.5				

Table 6 shows effect of clomiphene citrate in combination with different drugs in medical therapy. The rate of ovulation was 64% among those who were treated with Clomiphene citrate.

The rate of ovulation was 59% among those who were treated with Clomiphene citrate+metformin. The rate of ovulation was 45% among those who were treated with Clomiphene citrate+pioglitazone.

Thus, the ovulation rate was highest when treated with clomiphene citrate alone than the combination therapy. The rate of pregnancy was 9% among those who were treated with Clomiphene citrate. The rate of pregnancy was 13.2% among those who were treated with Clomiphene citrate+metformin. The rate of pregnancy was 12% among those who were treated with Clomiphene citrate+pioglitazone.

**Table 5: Ovulation rates in PCOS patients who underwent laparoscopic ovarian drilling (LOD).**

Characteristics	Category	Size n=200	Ovulation rate
Age in years	<30 years	175	78%
	>30 years	25	70%
Body mass index (kg/m <sup>2</sup> )	<29	110	81%
	30-34	76	84%
	>34	14	44%
Duration of Infertility	<3 years	154	90%
	3-6 years	30	83%
	>6 years	16	52%
Ovarian Volume	<14	166	80%
	>14	34	81%

**Table 6: Effect of clomiphene citrate in combination with different drugs in medical therapy.**

Drugs used	Ovulation in %	Pregnancy in %
Clomiphene citrate	64	9
Clomiphene citrate + metformin	59	13.2
Clomiphene citrate + pioglitazone	45	12

**DISCUSSION**

In the present study the incidence of infertility was 12.4%. The incidence of PCOS among these infertile patients was 10.5%. Dasgupta S et al, reported that 7-10% of infertile women patients as suffering from PCOS.<sup>8</sup>

In the present study, 127 had primary infertility and 73 had secondary infertility with PCOS. It was found that majority of the primary infertility with PCOS were from the age group of 20-25 years and secondary PCOS cases were in the age group of 25-30 years. It was found that

110 patients were overweight, 76 patients were grade one obese and 14 patients were grade two obese. PCOS women with BMI >34 kg/m<sup>2</sup> achieved significantly lower rates of ovulation after LOD compared with moderately overweight and normal overweight women.

The findings in the present study are in agreement with the previous reports by Gjonnaess H et al, who reviewed 252 patients who underwent LOD and found that women with marked obesity achieved significantly lower ovulation rates compared with women with normal and moderately elevated BMI.<sup>9</sup>

Hence weight reduction by decrease of diet and regular exercise was advised as the first line of treatment in obese patients with PCOS. This showed an increase in ovulation and pregnancy rates. This significant outcome with weight reduction can be compared to studies carried out by Moran LJ et al, where 44% increase in ovulation rates was seen with a daily diet of 600 JK/day and weight loss of 7.7 kg.<sup>10</sup>

In the present study, the menstrual disorder of the sample, 76 women had regular cycles, 106 had oligomenorrhea and amenorrhea was seen in 18 patients. Menstrual irregularities like oligomenorrhea and amenorrhea was seen in 18 patients. Menstrual irregularities like oligomenorrhea and amenorrhea were seen in association with chronic anovulation with PCOS by Frank S et al, and Goldzeiher JW et al.<sup>11,12</sup>

The incidence of oligomenorrhea in the present study was 53% which is comparable to studies done by Frank S et al, and Goldzeiher JW et al.<sup>11,12</sup>

Hyper androgenic features like acne was seen in 24% of the cases in the present study which is comparable to study by Frank S et al, Hirsutism was seen in 65% of the cases which is comparable to study report by Frank S et al, and Goldzeiher JW et al.<sup>11,12</sup> Insulin resistance was seen in 32.7% in non-obese and 70% of obese PCOS in the present study, which is in accordance with Glueck CJ et al, who reported that Insulin resistance was seen in 28% in non-obese and 75% of obese PCOS.<sup>13</sup>

These patients have shown marked improvement when advised for weight reduction and exercise. The percentage of ovulation and pregnancy was found to be 64% and 9% respectively in patients with PCOS after clomiphene citrate administration which can be compared to the studies conducted by Hammond G et al.<sup>14</sup>

Insulin sensitizers like metformin and pioglitazone when administered along with clomiphene citrate have shown to increase the ovulation rates by 59% and 45% respectively and pregnancy rates by 13.2% and 12% respectively which is comparable to the studies conducted by Zain MM et al, who reported that the ovulation rates with clomiphene citrate and clomiphene citrate plus metformin were 59% and 68.4% and the

pregnancy rates were 15.4% and 18.4% respectively.<sup>15</sup> PCOS was the most common cause of anovulatory infertility being found in 75% of the cases as per Hull MGR et al.<sup>16</sup> Laparoscopic ovarian drilling (LOD) has been widely used to induce ovulation in PCOS women with failure of treatment with clomiphene citrate.

Many authors have reported high ovulation rates of up to 80% following LOD like the one Gjonnaess H et al.<sup>9</sup> It was found that age less than 30 years responded well to LOD and had spontaneous ovulation rate of 78% and age of more than 30 years also ovulated spontaneously in the present study. This showed that increasing age has not much effect on ovulation induction by LOD.

## CONCLUSION

All patients presenting with complaint of infertility should be evaluated for menstrual irregularities like oligomenorrhea and amenorrhea, symptoms of hyperandrogenism like acne, androgenic alopecia, hirsutism and acanthosis nigricans, insulin resistance to be diagnosed as PCOS. Incidence of menstrual irregularities is high in women with PCOS. All women diagnosed to have PCOS should be evaluated for insulin resistance specifically if they are obese.

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