RESEARCH ARTICLE

STUDY OF 100 CASES OF INFERTILITY IN POLYCYSTIC OVARIAN SYNDROME AND ITS MANAGEMENT OUTCOME

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ABSTRACT

Background: With all the modern needs of contraception rising on one side, infertility is still a major challenge to the gynaecological practitioners on other hand. Polycystic ovarian syndrome (PCOS) is the most common cause of anovulatory infertility, being found in ~75% of cases. PCOS now proves to be a significant factor in female infertility with prevalence of 0.6 to 3.4% in infertile couples. With improving laboratory facilities, sonography and with routine laparoscopic evaluation of infertility, PCOS has shown a remarkable increase of incidence in recent years.

Aims & Objective: The diagnosis of PCOS by ultrasonography & investigations like LH, FSH, Prolactin and or Laparoscopy. The evaluation of treatment options like clomiphene citrate, metformin and laparoscopic ovarian drilling.

Material and Methods: This is a study of 100 cases of infertility with polycystic ovarian syndrome and its pregnancy outcome. In this study from May 2011 to April 2013,100 cases of Infertility with PCOS were studied at the tertiary care center. Hormonal assay, Ultrasound and laparoscopy were used for diagnosis. Clomiphene citrate, metformin and laparoscopic ovarian drilling were used as treatment modalities.

Results: In our study 58% patients were in the age group of 21-25 years and 100% patients complained of infertility among which 60% were of primary type. LH:FSH ratio was more than 1.6 in nearly 82% patients. Among all treatment modalities conception rate with Clomiphene citrate was 40%, with metformin it was 20% and with laparoscopic ovarian drilling followed by C/C it was 65%.

Conclusion: PCOS is emerging disease of the new generation found more in young adults being the leading cause of infertility. Apart from diet and exercise changes in lifestyle modification treatment is required in most patients with good conception rate with C/C and laparoscopic ovarian drilling.

Key-Words: Infertility; Polycystic Ovarian Syndrome (PCOS); Metformin; Clomiphene Citrate; Laparoscopic Ovarian Drilling

Introduction

Infertility, though not a physically debilitating disease, severely affects the couple's psychological harmony, sexual life and social function. With all the modern needs of contraception rising on one side, infertility is still a major challenge to the gynaecological practitioners on other hand. Polycystic ovarian syndrome (PCOS) is the most common cause of anovulatory infertility, being found in ~75% of cases.[1] PCOS is the commonest endocrine disease in women of reproductive age. It affects 5-10% of women of reproductive age.[2,3] It is associated with increased androgen secretion, hirsuitism, menstrual irregularities and infertility.[3,4] PCOS now proves to be a significant factor in female infertility with prevalence of 0.6 to 3.4% in infertile couples. With improving laboratory facilities, sonography and with routine laparoscopic evaluation of infertility, PCOS has shown a remarkable increase of incidence in recent years. As women with PCOS are at increased risk of diabetes, hypertension, cardiovascular disease, hyperestrogen related cancers.[3] It requires thorough evaluation & treatment.

Materials and Methods

Between May 2011 to April 2013, 100 patients with infertility with proved PCOS who came with chief complains of menstrual irregularities underwent study at the tertiary care centre. The detailed history and general, vaginal examination of patients carried out. Suspected cases of PCOS, send for ultrasonography & investigations like LH, FSH, and Prolactin. Laparoscopy is not must for diagnosis but it was carried out in selected patients resistant to medical treatment and also to rule out other cause of infertility.

The diagnosis of PCOS was based on the following

criteria (Rotterdam 2003 Consensus Workshop)[5]: (1) Oligo/or Anovulation (oligo/ amenorrhoea); (2) Clinical of hyper androgenaemia (Acne, Hirsuitism etc.) or Biochemical Signs (2nd day of menstruation) - Serum LH, Serum FSH, Serum LH/FSH ratio, Serum Prolactin; (3) There was ultrasonographic evidence of ovarian stromal hypertrophy and multiple (≥12), small (2-9 mm) follicles arranged periphery[6] and exclusion of other aetiologies (congenital adrenal hyperplasia, androgen secreting tumours, Cushing's syndrome) Recent management option for PCOS like Clomiphene Citrate, Metformin and Laparoscopic Ovarian Drilling has been evaluated. HSF study was carried out routinely to rule out associated male factor problem. In PCOS cases, Clomiphene Citrate given with starting dose of 25 mg/day rather than 50 mg/day on day 2 to day 6 or day 5 to day 9 after onset of menses.[7] Ovulation documented using TVS. Ovulation is usually expected to occur 5-10 days after last day of therapy. Injection HCG 5,000 IU i.m. given for follicular rupture.

Metformin given, 500 mg once a day with breakfast for 4 days ⇒ 500 mg twice a day with breakfast & dinner for 4 days ⇒ 500 mg with breakfast & 1000 mg with dinner for 4 days ⇒ Thereafter up to 1000 mg twice a day. It may take up to 2 months of therapy before spontaneous ovulation.[8,9]

Laparoscopic ovarian drilling: In most cases a three-puncture laparoscopy was performed. A monopolar coagulating current at 40 W power setting was used and the duration of each penetration was ~5 s. Three to 10 punctures were made in each ovary depending on its size, each measuring 4 mm in diameter and 7–8 mm in depth. At end of procedure lavage with copious amount of normal saline is given over ovarian surface. Hydro flotation with 500ml ringer lactate can minimize post-operative adhesion.

Treatment of Associated Factors: (a) Treatment of hyperthyroidism; (b) Treatment of oligospermia; and (c) Bromocriptin for hyperprolactinemia etc.

Results

Mean age Distribution in this series is 25 year it indicates that PCOS is a disease of young patients. All patients studied basically came with complaints of infertility followed by menstrual irregularities (Table 2). Most Patients, 35% have normal menses while 65% have menstrual irregularities. Majority of patients 70% have primary infertility. This signifies that incidence of primary infertility is high in patients of PCOS (Table 3). Typical polycystic ovaries appear enlarged on TVS but many women have normal looking ovaries too, so sonography findings should have be collaborated with clinical manifestation and other laboratory data. Laparoscopy could also add to diagnosis accuracy of PCOS (Table 4). Normal LH:FSH ratio is around 1 in early follicular phase (Table 5). Randomly selected 30 patients were treated with c/c as the first mode of therapy, 15 of them responded by ovulation (50%), with a period of 6 months. Success rate concerned with conception was only 20% showing disparity existing between ovulation and conception. Randomly selected 30 patients were treated with Metformin as the first mode of therapy, 21 of them responded by ovulation (70%), with conception rate of 23.3%, a period of 6 months. 40 patients were subjected to Laparoscopic Ovarian Drilling. Laparoscopic Ovarian Drilling resulted in higher ovulatory rate (80%) and conception rate (65%) (Table 6).

Table-1: Age Distribution of PCOS Cases

Age of Patients (Years)	Total No. of Cases	Percentage
Less than 20	04	4
Between 21-25	58	**58**
Between 26-30	36	36
More than 30	02	2

Table-2: Frequency of Complaints

Chief Complaints	Total No. of Cases	Percentage
Infertility	100	100
Menstrual irregularities	65	65
Acne, Hirsutism	15	15
Obesity	20	20

Table-3: Menstrual Patterns and Type of Infertility in PCOS

Characteristics		Total No. of Cases	Percentage
Menstrual History	Normal Menses	35	35
	Oligomenorrhea	40	40
	Irregular Cycle	23	23
	Amenorrhea	2	2
Types of Infertility	Primary	70	70
	Secondary	30	30

Table-4: Ultrasonography for PCOS

Ultrasonography	Total No. of Cases	Percentage
Enlarged Ovary	82	82
Normal Ovary	18	18

Table-5: LH:FSH Ratio

LH:FSH Ratio	Total No. of Cases	Percentage
<1	1	1
1-1.5	12	12
1.6-2	32	32
>2	55	55

Table-6: Outcome in Different Modality of Treatment

Modality of Treatment	Ovulatory Rate (%)	Conception Rate (%)	Abortion Rate (%)	Total (%)
Clomiphene Citrate	15 (50)	6 (20)	2 (6.7)	30 (100)
Metformin	21 (70)	7 (23.3)	1 (3.3)	30 (100)
Laparoscopic Ovarian Drilling	32 (80)	26 (65)	5 (12.5)	40 (100)

Discussion

PCOS affects 5-10% of women of reproductive age group.[2] In our study Mean age for PCOS in women is 25 years indicated that PCOS is a disease of young age. PCOS prevalence in infertile couples is about 0.6-3.4%. In this study all women are infertile with 70% women having primary infertility while 30% women having secondary infertility. Symptomatic women more often experienced Infertility. Oligomenorrhea or amenorrhea as well as obesity were more often associated with decreased fecundability. Spontaneous ovulation have been reported in up to 32% of ‘‘cycles.’’ In our study 35% patients have normal menstrual cycle while 65% of patients have menstrual Irregularities while other studies like Stephen Frank, Vaclav Insler and Rajan showed 80%, 50% and 51% menstrual Irregularities respectively. Women with oligomenorrhea or amenorrhea have about a 90% chance of being diagnosed with PCOS, and up to 95% of affected adults have oligomenorrhea or amenorrhea.[10] The definition used to establish the diagnosis of PCOS affects the proportion of women included with menstrual irregularities.[11] Amenorrheic women with PCOS usually have the most severe hyperandrogenism and higher antral follicle counts as compared with women presenting with oligomenorrhea or regular menstrual cycles. Menstrual cycles in women with PCOS become more regular as they approach menopause. Obesity rather than the menstrual cycle pattern or the size of the follicular cohort determines hyperinsulinemia, dyslipidaemia, and hypertension in aging women with PCOS. Lifestyle changes ,including diet ,exercise and behavioural modification improve metabolic and reproductive abnormalities of Obese patients with PCOS.[12] Not all women with the polycystic ovary syndrome (PCOS) on ultrasound (US) will have the syndrome, and clinical and biochemical features of PCOS or may be present without US features. In our study 82% patients of PCOS having enlarged ovaries while 18% of patients of PCOS having normal size ovary. The sensitivity of US in detecting PCOS was, therefore, determined in prospective study of Atiomo WU.[6] 72 women (32 PCOS and 40 controls). The most sensitive features were the presence of 10 or more follicles (82% and 69% in the left and right ovary) and a peripheral distribution of follicles (81.8% and 71.9% in the left and right ovary). Although ovarian enlargement and stromal brightness were not as sensitive as the previous criteria, stromal brightness was most specific. Combining all the criteria predicted a diagnosis of PCOS or control correctly in 86.4% of cases. This study shows that established US criteria of polycystic ovaries remain of value in the diagnosis of PCOS; however, the discrepancy between the left and right ovaries is an interesting but unexplained finding. Laparoscopy is not must for diagnosis but it was carried out in selected patients resistant to medical treatment and also to rule out other cause of infertility. In our study 48.8% patients undergone for Laparoscopic Ovarian Drilling. Both the absolute level of circulating LH and its relationship to FSH levels are significantly elevated in PCOS women as compared with controls.[13] This is due to an increased amplitude and frequency of LH pulse.[14] Elevated LH concentrations (above the 95th percentile of normal) can be observed in 60% of PCOS women, whereas the LH/FSH ratio may be elevated in up to 95% of subjects, if women who have ovulated recently are excluded. In our study 85% of patients having raised LH Normal LH value in follicular phase 5-20 mIU/ml, while 94% having normal FSH and only 6% having low FSH level. Normal FSH value in follicular phase 4.5-20 mIU/ml. Before any intervention is initiated, preconceptional counselling should be provided emphasizing the importance of life style, especially weight reduction and exercise in overweight women, smoking and alcohol consumption. The recommended first-line treatment for ovulation induction remains the anti-estrogen clomiphene citrate (CC).[14] With

Clomiphene Citrate, in our study ovulatory rate is 67%, conception rate 40% and abortion rate is 16.63%. Approximately 75–80% of patients with PCOS will ovulate after CC.[15] CC remains the treatment of first choice for induction of ovulation in anovulatory women with PCOS.[16] Cost of medication is low, the oral route of administration is patient friendly, there are relatively few adverse effects, little ovarian response monitoring is required and abundant clinical data are available regarding safety of the drug. With regard to the use of metformin for induction of ovulation, in our study ovulatory rate is 40%, conception rate 20% and abortion rate is 16.6%. In CC-resistant women, metformin plus CC led to higher live birth rates than CC alone.[17] The main indication for Laparoscopic ovarian surgery (LOS) is CC resistance in women with anovulatory PCOS.[18] LOS also may be recommended for patients who persistently hypersecrete LH, either during natural cycles or in response to CC, because it may reduce LH secretion. In addition, LOS may be useful in anovulatory women with PCOS who need laparoscopic assessment of their pelvis or who live too far away from the hospital for the intensive monitoring required during gonadotrophin therapy. Ovarian drilling by hydrolaparoscopy is an effective treatment for CC-resistant PCOS.[18] Extensive ovarian diathermy is not indicated to prevent hyperresponsiveness to exogenous gonadotrophins. In our study 80% ovulatory rate, 65% conception rate and 19.23% abortion rate achieved. In ~50% of LOS-treated women, adjuvant therapy will be required.[19] In these women, the addition of CC can be considered after 12 weeks if no ovulation is detected. Long-term adverse events potentially include adhesion formation and premature menopause.[20]

Conclusion

100 cases of proved PCOS 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 patient is 25 year suggesting it to be the disease of younger patients.

Majority of patients came with - infertility, menstrual irregularities (65%), Hirsutism (15%), Obesity (20%). 49% of PCOS women in this study had apparently regular menstrual cycles prior to treatment. Although chronic anovulation in women with PCOS is usually associated with menstrual irregularities (Franks, 1995), several authors have reported that 16–24% of these women do have apparently 'regular' menstrual cycles (Goldzieher and Axelrod, 1963; Naether et al., 1994; Balen et al., 1995; Carmina and Lobo, 1999). Furthermore, many anovulatory PCOS patients ovulate occasionally and some may resume regular menstrual cycles for variable periods of time. This explains why some anovulatory PCOS patients conceive spontaneously while being investigated for infertility or waiting for treatment. Incidence of Primary infertility is high in PCOS (60%). Ultrsonography (TVS) showed changes of PCOS in 82% while in remaining cases the ovaries appeared normal suggesting that anatomical variation is not to the pathophysiological mechanism behind the disease. Patients treated with Clomiphene Citrate showed ovulation rate of 67% and conception rate of 40%. Disparity between ovulation and conception in Clomiphene Citrate induced cycle is due to LPD (Luteal Phase Defect) and aged ovum. With Metformin showed ovulation rate of 40% and conception rate of 20%. Out of these abortion rate is 16.6%. Patients treated with Laparoscopic Ovarian Drilling showed ovulation rate of 80% and conception rate of 65%. This signifies that Laparoscopic Ovarian Drilling in PCOS cases improved both ovulation and conception compared to Clomiphene Citrate and Metformin.

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