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CLINICOPATHOLOGICAL CORRELATION OF POLYCYSTIC OVARIAN SYNDROME AND INFERTILITY IN 100 INFERTILE FEMALE CASES

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ABSTRACT

Infertility is considered as a matter of inequality and social injustice, along with a major health problem. Among the causes for female infertility, polycystic ovarian syndrome (PCOS) is the most common cause of anovulatory infertility, being found in ~75% of cases. It affects approximately 5-10% of women of reproductive age group. With the advancement in hormonal assessment techniques, endometrial biopsy and Ultrasonography, PCOS has shown a remarkable increase in its incidence in recent years.

OBJECTIVES: *To Diagnose the cases of PCOS by using triad of ultrasonography ,biochemical investigations like LH, FSH and Prolactin levels and endometrial biopsy and thus evaluating the correlation of PCOS and infertility and the preferred treatment line.*

MATERIAL AND METHODS: *This was a study of 100 infertile females (excluding the male factors) over a period of two years (2013-2015). Evaluation for PCOS was done using hormonal assay, ultrasonography and endometrial biopsy in a tertiary care hospital.*

RESULT: *In our study, ovulatory defects were seen in 37 cases (37%) which constituted maximum number of cases in female infertility. PCOS constituted 18 cases (48.6%) of the ovulatory defects, maximum in the age group of 26-30 years (38.9%), among which 72.2% were of primary infertility type. LH:FSH ratio was more than 1.6 in 88.9% of the PCOS cases. Maximum PCOS cases were correlating to the histopathological finding of anovulatory phase of endometrium and more than 50% were correlating with ultrasonographic finding of PCOS ovary.*

CONCLUSION: *PCOS was the most common cause of infertility among young females of new generation. Combination of change in life style modifications and treatment including clomiphene citrate can lead to better outcome.*

KEYWORDS : Hormonal assessment, Infertility, Polycystic Ovarian Syndrome, Ultrasonography.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is considered as amongst the most common causes of anovulatory infertility, being found in ~75% of cases.[1] PCOS is the commonest endocrine disease in women of reproductive age. It affects approximately 5-10% of women of reproductive age. [2, 3] It is associated with increased androgen secretion, hirsutism, menstrual irregularities and infertility.[3]

PCOS is a condition that originates possibly at the time of puberty due to interplay of various factors like obesity and excess of ovarian androgen production due to hyperinsulinemia ,intrauterine environment, genetic factors (both X-linked and autosomal dominant modes of inheritance) and disturbance to hypothalamic-pituitary-ovarian axis.

Obesity induces, through the path of insulin resistance, high levels of insulin related growth factors, these will stimulate theca cells to produce supra normal amount of androgens and reduce sex hormone binding proteins (SHBG) synthesis by liver cells, thereby raising the proportion of free circulating testosterone. The resulting androgen excess is considered to contribute to the presence of increased number of follicles in all stages, as well as arrested maturation of FSH sensitive follicles, leading to PCOS ovary. Arrested maturation of follicles leads to the absence of corpus luteum , thus resulting in absence of progesterone and ultimate increased action of estrogen leading to endometrial hyperplasia.

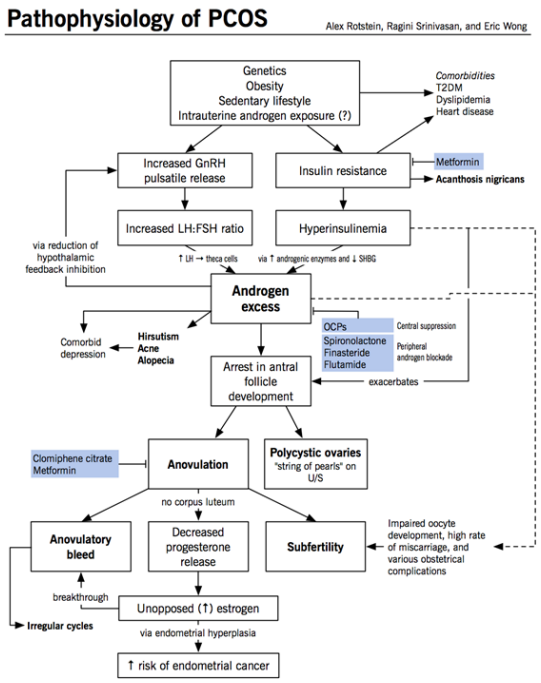

Figure 1: Pathophysiology of PCOS.

Thus, for the proper assessment of female infertility minimal work-up is required including serum levels of Prolactin, TSH, FSH, LH and assessment for polycystic ovary syndrome (PCOS) [4]. Estrogen effect on endometrium can be nicely examined through endometrial biopsies With the improving levels of laboratory facilities, sonography and other evaluation techniques including biopsies, this assessment has become quite easier and more precise resulting in remarkable increase in cases of PCOS in recent years. As women with PCOS are at increased risk of diabetes, hypertension, cardiovascular disease, hyperestrogen related cancers, so it requires thorough evaluation & treatment.

MATERIAL AND METHODS

In our study, 100 cases of female patients complaining of infertility and coming to tertiary care hospital were taken. Complete evaluation of patients were done with detailed history about active married life, menstrual history, obstetric and gynaecological history. As per the suspected causes, patients were sent for ultrasonography, hormonal assessment of LH, FSH, Prolactin and Thyroid profile and endometrial biopsy. For the clinical diagnosis of PCOS , following criterias were included (Rotterdam 2003 Consensus Workshop)[5]:-(1) Oligo/or Anovulation (oligo/ amenorrhoea); (2) Clinical signs/symptoms of hyper androgenaemia (Acne, Hirsuitism etc.) or Biochemical Signs (2nd day of menstruation) - Serum LH, Serum FSH, Serum LH/FSH ratio, Serum Prolactin; (3) Ultrasonographic evidence of ovarian stromal hypertrophy and multiple (≥12), small(2-9 mm) follicles arranged at periphery [6] and exclusion of other aetiologies (congenital adrenal hyperplasia, androgen secreting tumours, Cushing's syndrome). In PCOS patients, tablet clomiphene citrate was given on day 5 to day 9 after onset of menses [7] and ovulation was documented using sonography. Injection HCG 5,000 IU intramuscularly was given for follicular rupture. Treatment for the associated factors like for hyperthyroidism, hypothyroidism or hyperprolactinemia were also given.

RESULTS

Age (Years)	Total cases	Percentage (%)
18-22	6	6
23-27	25	25
28-32	50	50
33-37	13	13
38-42	6	6
Total	100	100

Table 1: Age distribution in infertility cases (100)

Total cases (%)	Ovulation Defects Cases (%)	Tubal defects Cases (%)	Uterus and cervical defects Cases (%)	Hormonal imbalance & others Cases (%)
Total(100)	37(37)	17(17)	14(14)	32(32)

TABLE 2: - Distribution of 100 cases of infertility as per the nature of disorder.

Characteristics		PCOS (18 cases out of total 100 cases) Distribution of cases	Percentage
Types of infertility	Primary infertility	13	72.2
	Secondary infertility	5	27.8

Table 3:- Type of Infertility in PCOS.

Age of patients	Number of cases	Percentage (%)
Less than 20	0	0
21-25	6	33.3
26-30	7	38.9
More than 30	5	27.8
Total	18	100

Table 4:- Age Distribution of PCOS Cases in female infertility

Chief complaints	Number of cases	Percentage (%)
Infertility	18	100
Regular menstruation	03	16.7
Menstrual irregularities	7	38.9
Acne , Hirsutism	3	16.7
Obesity	5	27.8

Table 5:- Frequency of Complaints in PCOS cases.

LH:FSH	No. of cases	Percentage (%)
Less than 1	0	0
1-1.5	2	11.1
1.6- 2	6	33.3
More than 2	10	55.6
Total	18	100

Table 6:- LH : FSH Ratio in PCOS cases in female infertility.

No.of cases (%) Total cases 18(100)	Clinical/usg/ hsg findings	Histopathological findings
2(11.1)	PCOS	Simple hyperplasia without atypia (image 2)
16(88.9)	PCOS	Proliferative phase(image 1)

Table 7:-(Clinical/radiological/HSG)-Histopathological correlation in PCOS (18 cases).

Ultrasonography	Cases	Percentage
Enlarged ovary	12	66.7
Normal ovary	6	33.3

Table 8:- Ultrasonography for PCOS.

DISCUSSION

Of the 100 cases of female infertility, maximum number of female infertility cases belonged to 23-32 years of age groups (75%) having 50% in 28-32 years and 25% in 23-27 years of age group. Our study was comparable to Zawar MP et al (2003) study which observed the maximum number of female infertility cases in 20-30 years of age group.[8]

Among the various cases, ovulatory defects were the most common disorder leading to infertility. In this study, 37% cases had ovulatory dysfunction and among these defects, PCOS was the most common cause. This was comparable with Sudha G. et al (2013)[9] study showing ovulation defects (50.07%) dominating over other disorders.

In this study of PCOS cases, primary infertility constituted 72.2%. This signified that incidence of primary infertility was high in patients of PCOS. Present study was comparable with Dhagat V et al study of 100 cases of infertility in polycystic ovarian syndrome and its management outcome (2013) having 70% and 30% cases of primary and secondary infertility respectively [10].

PCOS affected women of reproductive age group . In this study, maximum and minimum number of PCOS cases were seen in 26-30 years of age (38.9%) and less than 20 years (0%) respectively. In contrast, Dhagat V. et al study of 100 cases of infertility in polycystic ovarian syndrome and its management outcome (2013) , maximum number and minimum number of PCOS cases were seen in 21-25 years of age (58%) and more than 30 years (2%) respectively.[10] This discordance was due to different sample size (small sample size in present study). In present study, out of 100 cases of female infertility, 18 cases had PCOS while in Dhagat V. et al study all 100 cases studied had PCOS.

Symptomatic women more often experienced infertility. Oligomenorrhea or amenorrhea as well as obesity were more often associated with decreased fecundability. In this study, menstrual irregularities were the most common presenting

complaint in 38.9% PCOS cases of female infertility 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 90% chance of being diagnosed with PCOS, and up to 95% of affected adults have oligomenorrhea or amenorrhea.[11]

Not all women with PCOS on ultrasound will have the syndrome, and clinical and biochemical features of PCOS or may be present without sonography features. In our study 66.7% patients of PCOS had enlarged ovaries while 33.3% of patients of PCOS had normal sized ovary. The sensitivity of ultrasound in detecting PCOS was, therefore determined in prospective study of Atiomo WU, 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).

In our study LH:FSH ratio was more than 1.6 in 16 cases(88.9%) as compared to ratio of around 1 in normal follicular phase. This was due to more raised LH level and relatively low level of FSH in follicular phase. Present study was comparable with Dhagat V et al (2013) which showed maximum number of female infertility cases having LH: FSH ratio more than 2 (55%).[10]

While doing histopathological correlation, 88.9% of the PCOS cases were having endometrium in proliferative phase indicative of anovulatory cycle.

The recommended first line of treatment for PCOS is clomiphene citrate (CC). Approximately 75–80% of patients with PCOS will ovulate after CC.[12] In CC-resistant women, metformin plus CC led to higher live birth rates than CC alone.[13] Ovarian drilling by hydrolaparoscopy is an effective treatment for CC-resistant PCOS.[14] In ~50% of laproscopically treated women, adjuvant therapy will be needed.[15] In such cases, 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.[16]

CONCLUSION

Of the 100 cases of female infertility, ovulatory defects played the major role in infertility. PCOS was the leading cause of ovulatory dysfunction, affecting mainly females of age group 26-30 years and were mainly of primary type. Majority of females came with complaint of infertility and menstrual irregularities followed by obesity, acne and hirsutism. Among the diagnosed cases, not all the cases were showing PCOS findings on ultrasonography, 66.7 % were showing PCOS finding while another 33.3% were showing normal ovaries suggesting that anatomical variation was not directly linked to the pathophysiological mechanism behind the disease. Nearly all the PCOS cases were correlating to the histopathological finding of anovulatory phase of endometrium. The recommended line of treatment for PCOS includes clomiphene citrate. Resistant cases should be treated with metformin or laproscopic ovarian surgery in combination with clomiphene citrate.

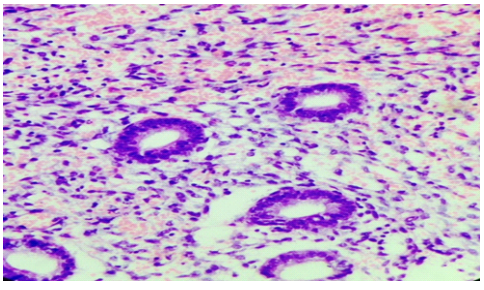

IMAGE 1: H & E, 10X, ENDOMETRIUM IN PROLIFERATIVE PHASE.

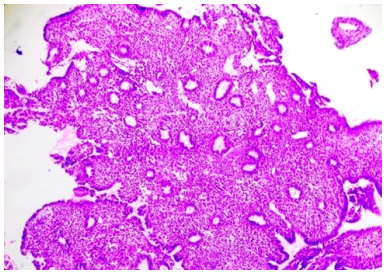

FIGURE 2: H& E, 10X, ENDOMETRIUM IN SIMPLE HYPERPLASIA WITHOUT ATYPIA.

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