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Pregnancy Outcome in Patients Conceiving after Management of Polycystic Ovarian Syndrome

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OBJECTIVE - To find out whether pregnancies resulting from treatment of polycystic ovarian syndrome (PCOS) run a higher risk of adverse outcome. **METHODS -** After making the diagnosis of PCOS based on predetermined criteria in 185 patients a standard management protocol was followed. Conception was achieved in 48 of them. Outcome of these pregnancies was compared with a matched control group comprising of 50 primigravidas without any risk factor. **RESULTS -** It was observed that the pregnancy wastage rate was significantly higher in the study group ($p < 0.05$). The clustering of wastage was in the first trimester suggesting an abnormality in the embryo, implantation or corpus luterum. **CONCLUSION -** Possible causes of adverse outcome can be obesity, insulin resistance, abnormal LH levels and hyperandrogenemia. A strategy to address these factors is essential to achieve a better pregnancy outcome in PCOS.

Key words : PCOS, pregnancy wastage.

Introduction

Polycystic ovarian syndrome (PCOS) is the commonest cause of ovulatory dysfunction in reproductive age group and has remained a challenge to its complete understanding and effective treatment. The morphological abnormality of multiple small follicles in the ovaries has deeper endocrinological disorder as part of etiopathogenesis of this disease. Achievement of fertility remains the goal in most of these patients. Various ovulation inducing regimens have been tried successfully to achieve ovulation and conception. However, the goal of establishment of a pregnancy is to take the pregnancy safely to term and delivery and it is not always met. Hence, it was decided to study how the pregnancies following PCOS fare vis-à-vis a control group.

Material and Method

This is a prospective analysis of all cases of PCOS treated between July, 1997 and June 2000. The criterion for diagnosis of PCOS in an infertile woman was the presence of any two of the following –

1. Clinical features of oligomenorrhoea / obesity / hirsutism.
2. Endocrinological feature of D3 LH>FSH
3. Sonological features of increased ovarian volume and or peripherally arranged multiple small follicles.

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All the patients had undergone the full infertility work up. Presence of any other factors causing infertility was taken as a criterion of exclusion to preempt their influence on the ultimate results.

All the patients with PCOS were subjected to ovulation inducing drugs by the following protocol -

1. Clomiphene citrate (CC) 100 mg OD from D3-D7 for two cycles.
2. In case of failure to achieve ovulation conception with above, CC in the same doses from D2-D6 were supplemented with Inj metrodin 75 IU from D6-D8 for two cycles.

If there was no positive response, the patient was subjected to laparoscopic fulguration of the ovaries and step 2 was repeated.

Follicular monitoring by transvaginal ultrasound was done in the cycles under study and intrauterine insemination performed on demonstration of ovulation. Forty-eight patients who achieved a pregnancy were followed up and were called Group A patients (Study Group). Group B (control Group) comprised of 50 randomly selected primigrvidas who had reported immediately after the first missed period. Care was taken to match the patients with respect to age of the patients of group A. Identification of any medical disorder at the first visit was taken as a criterion of exclusion.

Following parameters were taken as outcome measure

1. First trimester problems of sonological abnormalities, abortions and ectopic pregnancy.

2. Second trimester problems like identification of a congenital anomaly or occurrence of spontaneous abortion.
3. Third trimester development of PIH, hyperglycaemia, IUGR, preterm delivery and neonatal outcome.

Taking all the above into consideration overall pregnancy wastage between the two groups were compared.

Out of 880 cases of infertility 185 (21.02%) had PCOS and out of these 48 (25.9%) achieved pregnancy with treatment - 32 with CC, 10 with CC+ metrodin and 6 following laparoscopic fulguration.

The mean age of PCOS patients was 25.2 years with a range of 23 to 28 years.

The average time taken for pregnancy (TTP) after marriage for PCO cases was 4.7 years and for the control group 1.2 years. Pregnancy events in the first, second and third Trimesters have been summarized in Table I, II and III respectively. Table IV compares the total pregnancy wastage and take home baby (THB) rates between group A and B.

Discussion

Incidental or isolated finding of polycystic ovaries must be distinguished from the diagnosis of polycystic ovarian syndrome (PCOS). Whereas the former denotes an ultrasonographic finding, it has to be associated in the latter with infertility, oligomenorrhoea, obesity, hyperandrogenic features and / or biochemical features like raised LH, insulin, and androgen as reviewed by Rajkhowa et al[1]. Clayton and Ogoen[2] and Polson et al[3] reported that the finding of polycystic ovaries in an unselected female population is approximately 20%. However, the diagnosis of PCOS is tenable in less than 10% in such unselected population[4]. Among the infertile patients the incidence will be definitely higher which has been reported to be up to 50% by Sagle et al[5] among patients reporting to IVF clinics. It was found to be 21.02% in our series using the diagnostic criteria mentioned earlier. Various ovulation induction protocols have been used for patients with PCOS. We have restricted our protocol to the use of medical management for four cycles before subjecting the

Table I : First Trimester Events

Events	Group A (n=48)		Group B (n=50)	
	Number	%	Number	%
USG abnormality	6	12.5	2	4
Bleeding	8	16.6	5	10
Spontaneous abortion	6	12.5	4	8
Missed abortion	6	12.5	1	2
Total first trimester wastage	12	25	5	10

Table II : Second Trimester Events

Events	Group A		Group B	
	No	%	No	%
Termination for congenital malformation	1	2.08	1	2
Evidence of cervical incompetence	1	2.08	1	2

Table III : Third Trimester Events

Events	Group A (n=48)		Group B (n=50)	
	No	%	no	%
PIH	3	6.25	2	4
IUGR	4	8.33	4	8
Hyperglycamia	4	8.33	1	2
Preterm Delivery	3	6.25	2	4
Term Delivery	32	75	41	82
Instrumental delivery	2	4.16	2	4
Ceserian	8	16.66	6	12
Birth Asphyxia	1	2.08	1	2

Table IV : Pregnancy Wastage

Event	Group A (n=48)		Group B (n=50)	
	No	%	No	%
First Trimester Wastage	12	25	5	10
Total Pregnancy Wastage	13	27.08	6	12
Take Home Baby	35	72.91	44	88

patients to laparoscopic fulguration which is considered as a viable alternative with relatively longer effect. The cumulative pregnancy rates in the PCOS patients has been found to be 25.94% in our study.

Pregnancy outcome of PCOS patients has been a matter of concern[6]. While analyzing the causes of recurrent abortion Regan et al[7] reported a raised level of LH in follicular phase in 9 out of 30 patients. Sagle et al[5] have also reported the finding of PCO in a large number of recurrent abortion patients even if LH was not always raised. The factors responsible for recurrent abortions were operative in them in the first pregnancy as well. Hence in our series the outcome of the first conception in PCOS patients has been taken into consideration and a pregnancy wastage of 27.08% has been encountered which is significant when compared to that in control group ($p<0.05$). The significance of the difference between both the groups is mostly applicable to the first trimester loss (25% vs. 10%, $p<0.05$).

Raised LH level in the follicular phase can affect the quality of the ovum and resultant embryo[7]. Hyperandrogenemia acting on the oocyte and endometrium can also be responsible for poor implantation as suggested by Watson et al[8]. This hyperandrogenic environment is largely unaffected during ovulation induction with any drug. An important observation in our series is that only one out of six pregnancies occurring after laparoscopic fulguration ended in an abortion (16.6% as against 25% for the whole study group). The reduction in the androgenic environment after laparoscopic fulguration may have been helpful.

Regarding the role of obesity it has been pointed by Fairley et al[9] that even moderately obese PCOS patients who are on stimulation with gonadotrophin experience high miscarriage rates. Obesity is present in 35% of PCO patients and Kiddy et al[10] have found that reduction of weight improves the reproductive outcome. Chang et al[11] have shown the presence of hyperinsulnemia in non-obese PCOS patients to demonstrate that this is a feature specific to PCOS rather than secondary to obesity. In our series the only difference of significance in late pregnancy was the occurrence of random hyperglycaemia in four patients in the study group against one in the control group, though there was no case of impaired GTT. All our patients were euglycemic before pregnancy. Insulin resistance being a basic

abnormality in PCOS, presence of hyperinsulinemia is also likely to have a bearing on pregnancy wastage.

There is no doubt that the chances of an adverse pregnancy outcome is higher in PCOS patients in comparison to the general population. Hence the preventive strategy would call for tackling the possible etiological factors before conception. Scope of reduction of weight should always be considered. Use of metformin for few months prior to induction of ovulation has been advocated. Some of the recent work by Glueck et al [12] goes on to suggest that continuation of metformin during pregnancy is not only safe but also reduces pregnancy losses. Hamburg et al[13] as well as Johnson and Pearce [14] have reported independently that pituitary suppression with LHRH analogue followed by stimulation with exogenous gonadotrophin, though expensive, can deal with the problem of high endogenous LH levels. Fulguration or even simple multiple puncture of the polycystic ovaries during laparoscopic evaluation can also reduce the androgenic milieu and favor the subsequent pregnancy outcome.

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