PERINATOLOGY OF INFERTILE COUPLE

by

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My interest in investigation and treatment of infertile couple dates back to August, 1975, from which period over 7 years 2086 couple were investigated on a standard protocol. The various therapeutic approaches included pelvic infertility surgery, induction of ovulation with clomiphene, gonadotropine, corticosteriods and bromocriptine, treatment of cervical and uterine factors and conservative approach to subjects with 'unexplained infertility'. On the male side the range of treatments offerred was varicocele correction, anastomotic surgery for the accessory ducts, Gonadotropin and clomiphene therapy for oligospermia and artificial husband insemination (AIH) for sexual disorders. In addition another 428 couples were recruited for aritifical donor insemination (AID) wherein the barren union was due to intractable seminal defficiency.

While the out-come of various treatment regimes for both male and female infertility groups have been illustrated in the previous publications (Rajan, 1976, 1977, Rajan and Rosamma John, 1978, Rajan and Joseph, 1979, Rajan and Usha, 1980, Rajan *et al*, 1981, Rajan and Ambika Devi, 1982 and Rajan *et al*, 1982), this is the first time that an attempt is made at reviewing the pregnancy course and outcome in the infertile subjects. However, since the pregnancy complications of AID subjects have been already dealt with in detail (Rajan, 1982) the same will not be included in this communication. Instead, the pregnancy course and outcome for the subjects treated for male factors, female infertility or unexplained pathology alone will be reviewed in detail.

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Material and Methods

As previously mentioned in the AID series, it is very difficult to review the pregnancy course and outcome in infertile subjects achieving a conception. Nontheless, it is worthwhile knowing as to how many of the infertile couples achieved their goal of parenting healthy children and how many met with obstetric accidents and perinatal loss. This will also give an insight into the incidence of pregnancy wastage and foetal loss which can be compared with the general incidence. Whether the nature of delivery, weight of the new born and the pregnancy complications differ in anyway from the control group also be evaluated.

The reasons for incomplete data on the perinatal outcome in infertile subjects are many. The foremost is the referral system. More than 90% of the couples undergoing infertility work-up under the author report from distant places referred by the gynaecologists or general practitioners. After completing the investigations and treatment the patients go back to there referred physicians, and even the occurrence of pregnancy may not be always

reported. However, in groups who had undergone pelvic surgery or polonged treatment for anovulation or male factors, pregnancy is quite promptly reported either by the couple or by the referring physician. Even in this group the further details about the pregnancy course and outcome are not always available. Moreover, we are not offering obstetric service for all our infertile subjects achieving pregnancy.

The above mentioned limitations will explain why data could be collected from 321 subjects becoming pregnant following investigation and treatment of infertility problems. These pregnancies have resulted following one of the treatment schedules, namely, (i) conservative management of 'unexplained infertility', (ii) treatment of female factors which include tubal and other pelvic factors, anovulation, cervical and uterine factors, and (iii) treatment of male disorders such as varicocele with oligospermia, medical treatment of oligospermia, obstructive azoospermia and sexual disorders. The number of pregnant subjects in the different treatment groups are given in Table I.

TABLE I
Pregnancies Following Treatment of Infertility

Aetiology of infertility and treatment	No. of patients achieving conception
UNEXPLAINED INFERTILITY:	
Conservative treatment	143
Clomiphene therapy	35
Laparoscopy	6
'Fertility' laparotomy	5
FEMALE INFERTILITY:	
Induction of ovulation with clomiphene citrate	31
Hyperprolactinaemia treated with bromocriptine	5
Congenital adrenal hyperplasia (corticosteroid)	1
Wedge resection of ovaries	2
Surgical treatment of endometriosis	12
Uterotubal implantation	7
Myomectomy	6
Asherman Syndrome	2
Salpingolysis	1
Bilateral salpingostomy	1
Unilateral salpingo-ovariotomy (ovarian tumour)	1
Hymenectomy	1
Resection of vaginal septum	1
MALE INFERTILITY:	
Oligospermia (varicocelectomy)	23
Oligospermia (H.C.G. therapy)	13
Oligospermia (clomiphene therapy)	13
Oligospermia (H.C.G. and clomiphene)	6
Obstructive azoospermia (anastamosis)	3
A.I.H. for impotence	2
TOTAL	321

Pregnancy Course and Outcome

Among the 321 patients reporting pregnancy, the obstetric outcome could be completely evaluated in 99 subjects, only antenatal follow-up could be made in 205 subjects and the remaining 17 patients could not be following. The antenatal follow-up and the obstetric outcome including the pregnancy complications are documented in Table II. Among the total

TABLE II

Pregnancy Course and Outcome in 321 Infertile Subjects

Details of pregnancy	No. of subjects
Pregnancy followed upto first trimester	113
Pregnancy followed upto mid trimester	67
Pregnancy followed upto last trimester	25
Vaginal delivery of healthy babies	39
Caesarean section for healthy babies	30
First trimester abortion	20
Mid trimester abortion	5
Multiple pregnancy	2
Breech presentation	1+1 (caesarean)
Intra-uterine death	1
Ectopic gestation	1
Pregnancies not followed	17

patients whose obstetric outcome was known, 39 patients underwent caesarean section and 39 were delivered vaginally and all of them carried home a healthy baby. The sex ratio for the healthy babies for male and female was 21:13. The birth weight of the new born ranged from 2.2 to 4.5 kg, with a mean of 3.25 kgs. About 75 per cent of the babies were weighing 3 kg or more, with only two babies weighing below 2.5 kgs.

A good number of patients could be followed for their pregnancy course upto first trimester (113), second trimester (67) and third trimester (25), and there were no antenatal complications in these subjects to the date of follow-up. However, their perinatal outcome is not known. Among those women in whom the perinatal outcome was known the obstetric complications encountered include: (1) abortions, (2) ectopic tubal gestation, (3) multiple pregnancy with neonatal loss, (4) intrauterine death, (5) breech presentation, (6) placenta praevia, (7) uterine scar dehiscence, and (8) manual removal of placenta. In addition to the obstetric complications there were 2 instances of clinically significant congenital anomalies in the live babies born. Yet another antenatal complication encountered was eclampsia in the patient who had multiple pregnancy (Table III).

TABLE III

Pregnancy Complications in Infertile Subjects

First trimester abortions	20
Mid trimester abortions	5
Multiple pregnancy with perinatal loss	2
Intra-uterine death	1
Pre-term labour (premature neonatal death in twins)	1
Term still birth (twins)	1
Eclampsia (twins)	1
Ectopic tubal gestation	2
Breech presentation	2
Placenta praevia	1
Uterine scar dehiscence	1
Manual removal of placenta	1
Congenital malformation of foetus	2

1. *Abortions*: Twenty subjects aborted in the first trimester and another 5 in the midtrimester. As could be seen from Table IV, which gives the incidence of abortion in the different treatment groups, ovulation induction or regulation with clomiphene has been found to be associated with greater incidence of abortions.

TABLE IV
Incidence of Abortion in the Different Treatment Groups

Treatment group	Total pregnancies	No. of abortion
Clomiphene for induction or regulation of ovulation	66	7
Spontaneous conception in 'unexplained infertility'	143	6
Oligospermia (clomiphene)	13	3
Endometriosis (surgery)	13	2
Utero-tubal implantation	7	2
'Fertility Laparotomy'	5	2
Varicocelectomy	23	1
Vaginal septum—resection	1	1
Congenital Adrenal hyperplasia treated with dexamethasone	1	1

Significant incidence is contributed by the small series of tubal implantations and surgery for endometriosis. Treatment of oligospermia with clomiphene is another group in whom the abortion rate appears to be high, especially when one considers the small number treated. Eventhough certain particular treatment groups showed a higher incidence of abortion, the overall incidence is certainly comparable to the incidence in the general population.

2. *Ectopic Gestation*: There was 1 case of ectopic tubal gestation recognised in this series of 32 pregnancies. This was a 30 year old patient with secondary infertility (first child alive) of 13 years duration. She conceived following the basic infertility work-up, and was diagnosed to have ectopic gestation when she was having 3 months amenorrhoea. Laparotomy revealed tubal rupture on the left side. She made uneventful recovery. The right tube was reported to be having adhesions.

While incidence of ectopic gestation is generally reported to be high following tubal surgeries and other pelvic infertility surgeries, todate we have hot encountered tubal pregnancies in our series of tubal surgeries or surgery for endometriosis.

3. *Multiple pregnancy*: There was 1 case of twin pregnancy in this series, and this patient conceived spontaneously following the investigations. She had not taken any drugs during the investigations. At 7th month she was admitted with imminent eclampsia and shortly developed convulsions. She delivered two premature infants and both succumbed to prematurity. Patient developed puerperal psychosis and was subsequently cured, and after this episode she was lost to follow-up.

Another patient had twin pregnancy following ovulation regulation with clomiphene citrate. Her husband was being concurrently treated for oligospermia with gonadotropins and clomiphene citrate. Her pregnancy reached term but ended in still birth.

Altogether there were 2 subjects with multiple pregnancy and both lost the babies in the form of neonatal death or still birth, of which one was following clomiphene therapy.

4. *Intrauterine death of foetus*: One 26 year old female with infertility duration of 1 year conceived spontaneously following investigations and developed growth retardation at 30 weeks and delivered a macerated foetus.

5. *Breech presentaion*: There were 2 instances of breech presentation in this

series, 1 was delivered vaginally and other by caesarean section. Both babies were born alive and healthy.

6. *Placenta praevia*: On 2 occasions indication for performing caesarean section was antepartum haemorrhage. Both were cases of minor degress of placenta praevia. One was a subject who had surgical treatment for endometriosis and the other patient had a spontaneous conception. In the former the baby weight was 3.6 Kg and in the latter 2.2 Kg, and both babies were alive and healthy.

7. *Uterine scar dehiscence*: Eventhough the maternal or foetal outcome was not compromised, scar dehiscence was a complication observed in 1 of the patients undergoing uterotubal implantation for bilateral proximal tubal block and subsequently achieving a conception. The scar dehiscence was observed at the time of caesarean section and the baby was born alive and healthy with no maternal complications.

8. *Manual removal of placenta*: Third stage complication in the form of retained placenta necessitating manual removal was encountered in 1 subject who conceived spontaneously following evaluation. The perinatal outcome was good in this patient.

9. *Congenital anomalies in the foetus*: In this group, 2 infants had congenital anomalies and both of them were clinically significant variety amenable to surgical correction. One was ileal atresia which was surgically corrected with no postoperative complications, and this baby was born to a mother in whom ovulation was induced by clomiphene citrate. The other was a case of cleft lip where conception occurred following treatment of oligospermia with clomiphene citrate.

Perinatal Mortality: Among the pregnancies that could be followed for perinatal outcome, the results were good in 69 subjects who went home with healthy babies, pregnancy wastage in the form of abortion was recorded in 25 subjects, and perinatal foetal loss occurred in 3 patients. Perinatal mortality was contributed by twin pregnancy in 2 subjects and intrauterine foetal death in 1 subject. One of these twin pregnancies was conceived following ovulation regulation by clomiphene citrate and concurrent male treatment for oligospermia with clomiphene citrate.

Repeat Pregnancies: Seven patients in whom the first pregnancy was lost in the form of abortion reported subsequently with second pregnancy. In this group, there were 2 subjects who had undergone utero-tubal implantation for proximal tubal block, and all the other subjects were those with no explainable cause for infertility. One of the patients who had utero-tubal implantation had 3 consecutive abortions in the second and first trimesters, and after the third abortion she could not be followed. (Table V).

Discussion

Eventhough the data presented on the perinatology of infertile subjects is incomplete in a wider perspective, some meaningful observations could be made in some aspects of infertility management. One important observation made that could be clinically significant is the higher incidence of pregnancy wastage, perinatal mortality in the form of still birth at term in twin pregnancy and congenital anomaly identified in the group in whom clomiphene citrate was employed for either induction or regulation of ovulation. Surprisingly, pregnancies following treatment of oligospermia with clomiphene citrate also have recorded a higher incidence of abortion; one of the congenital anomalies

TABLE V
Repeat Pregnancies in Infertile Women

No.	Treatment group	Termination of first pregnancy	Follow-up of subsequent pregnancy
1.	Spontaneous conception	First trimester abortion	2nd preg. normal
2.	Spontaneous conception	First trimester abortion	2nd preg. normal
3.	Clomiphene therapy	Second trimester abortion	2nd preg. normal
4.	Uterotubal implantation	Second trimester abortion	2nd and 3rd abortions
5.	Fertility laparotomy	First trimester abortion	2nd normal delivery 3rd normal pregnancy
6.	Uterotubal implantation	First trimester abortion	2nd preg. Nommal
7.	Fertility laparotomy	First trimester abortion	2nd normal pregnancy

(cleft lip) was also seen in this group, and the husband of the patient who had twins still birth also was being treated with clomiphene citrate at the time of conception. However, such pregnancy complications were not encountered in the series of oligospermia treated with gonadotropins (HCG) or varicocelectomy, eventhough these patients also had severe oligospermia and asthenospermia. This fact disproves the possibility of abnormal male gametes being responsible for the pregnancy complications.

Another group where higher incidence of abortions was recorded consisted of patients undergoing utero-tubal implantation for proximal tubal block and surgery for endometriosis. Contrary to expectation no tubal gestations were recorded in subjects undergoing tubal surgeries or other forms of infertility surgeries. Scar dehiscence is a potential risk to which a patient is exposed to if she conceives following utero-tubal implantation.

Nonetheless, considering all the pregnancy complications and the perinatal outcome, one does not feel that there is a higher incidence of complications in infertile subjects as is generally anticipated. This data on pregnancy complications compares favourably with that of the general incidence of pregnancy wastage and perinatal complications.

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