PREGNANCIES OF INFERTILE COUPLES

By

R. RAJAN

SUMMARY

Pregnancies ocurring in 349 infertile subjects following investigation and management of various forms of fertility disorders, reported over a period of 3 years, have been reviewed for pregnancy complications. The overall incidence of pregnancy complications is 16.33% and is comparable to the general incidence, and on this score a very rigorous pregnancy surveillance and monitoring are not needed as a routine. However, the high incidence of certain types of pregnancy complications such as ectopic gestation (1.43%), fetal anomaly (0.57%) and multiple pregnancy (0.57%) is important. Which type of infertile subject achieving a conception will need what type of pregnancy surveillance could be reasonably discerned from this study.

Ectopic gestation is exclusively encountered in 'unexplained infertility' subjects achieving spontaneous conception following laparoscopy (7.14%) or HSG (3.85%), and uterotubal implantation (8.33%). Subjects treated for ovulation induction, male factor, AID and surgical correction of endometriosis are not at high risk for ectopic gestation.

Fetal anomalies, (NTD and VSD) were purely a complication of induction of ovulation (2.00%), so also multiple pregnancy (2.00%).

Risk of abortion ranges from 5.41% (oligospermic subjects), 10.00% (anovulatory subjects), 10.83% (unexplained infertility), 14.93% (pelvic surgery) to 26.32% (AID). Lowest pregnancy complication (5.41%) in oligospermia treated group is noteworthy, and this proves, despite a poor pregnancy rate, the conceptions achieved are effected by the best quality sperms. The high incidence of abortions in AID warns against improper handling of semen sample, particularly increased collection-to-insemination interval.

Introduction

Conceptions following infertility treatment are generally considered to be at high risk for pregnancy complications particularly in the first trimester. This could be either due to the inherent risk factor in the female partner such as the advanced age, altered tubal anatomy,

From: Medical College, Kottayam.
Accepted for publication on 7-7-87.

associated uterine pathology and medical disorders, or just an exaggeration of the real situation by the very careful early pregnancy monitoring of these subjects. In our recent study on sonographic surveillance of early pregnancy in 81 infertile subjects (Rajan and Rajan, 1987) we recorded a pregnancy complication in 13 58% a figure which compares well with the general incidence. A more evident and significant observation of this study was the high incidence of ectopic gestation (2.47%), and hence we felt that the nature of pregnancy disorder was more of an indication for careful early pregnancy surveillance than the total incidence of pregnancy complications.

The present study is devoted to analysis of incidence and nature of pregnancy complications encountered in 349 infertile subjects reporting pregnancy over a period of 3 years from September, 1983 to December, 1986. These 349 pregnancies have been conceived following treatment of different types of fertility disorders, which could be broadly classified as: (i) unexplained infertility (conceptions following clinical evaluation, HSG or laparoscopy)...120 (38.34%), (ii) Ovulatory disorders (treated with clomiphene citrate, bromocriptin, dexamethasone and gonadotropins)...100 (28.65%), (iii) Pelvic infertility surgeries (endometriosis, uterotubal implantations, myomectomy, operative laparoscopy and pelvic adhesiolysis)...67 (19.20%), (iv) Male subfertility and correction of oligospermia (varicocele ligation, clomiphene therapy, HCG and hCG and hMG therapy)...37 (10.60%), (v) Artificial donor insemination (AID)...19 (5.44%) and (vi) miscellaneous (includes treatment of Asherman's Syndrome, vaginal septum excision and fertility counselling)...6 (1.72%).

Story Design

Infertile couples investigated and treated in our service were advised to report pregnancy at the earliest. Since March, 1985, sonographic evaluation is preferred and hence the patient is advised to report for scanning as early as 5th to 7th day of missed menstrual date (Rajan and Rajan, 1986). Further follow-up of pregnancy was either at our service or by the local Obstetrician, and pregnancy outcome was recorded.

Observations

Among the 349 subjects reporting pregnancy following infertility work-up and treatment pregnancy complications were recognised or reported in 57 subjects (16.33%). These complications included first trimester abortions in 40 subjects (11.46%), Ectopic tubal gestation in 5 subjects (1.43%), multiple pregnancy, fetal anomaly, intrauterine death and growth retardation for 2 subjects or 0.57% in each category and neonatal death in 4 subjects (1.15%).

The total 349 subjects were broadly classified into 6 groups and the pregnancy complications were evaluated in each group separately:

(i) *Unexplained Infertility*: There were 120 conceptions that have resulted following either a basic infertility work-up or HSG or laparoscopic evaluation. These spontaneous conceptions that followed the investigative procedures recorded abortions in 13 subjects (10.83%), ectopic gestation in 4 subjects (3.33%), and IUGR in one subject (0.83%). The overall complication rate was 15.00%, i.e., 18 pregnancies (Table I).

TABLE I
Spontaneous Conception in 'Unexplained Infertility'
(Total conceptions: 120)

Investigation	Total pregnancies	Abortions No. & %	Ectopic No. & %	IUGR. No. & %	Total No. & %
Clinical	52	7 (13.46)	nil	nil	7 (13.46)
Laparoscopy	42	4 (9.52)	3 (7.14)	nil	7 (16.67)
H.S.G.	26	2 (7.69)	1 (3.85)	1 (3.85)	4 (15.38)
Total	120	13 (10.83)	4 (3.33)	1 (0.83)	18 (15.00)

(ii) *Ovulation Induction*: Among the 100 conceptions following induction of ovulation by various ovulogens 17 pregnancies (17.00%) proved to be abnormal. The abnormalities included: Abortion (10.00%), Twins (2.00%), fetal anomalies (2.00%), IUGR (2.00%), and IUD (1.00%) (Table II).

(iii) *Conservative pelvic surgery*: Amongst 67 pregnancies following infertility surgeries, such as conservative surgery for endometriosis or inflammatory disease, uterotubal implantation or proximal tubal occlusions, myomectomy and operative laparoscopy (Table III), there were 12 (17.91%) pregnacy complications which included abortion in 10 subjects (14.93%), ectopic gestation in 1 (1.49%), and NND in 1 (1.49%).

(iv) *Treatment of oligospermia*: Among the 37 subjects who had conceived following correction of husband's oligospermia the only complication observed was abortion in 2 (5.41%) (Table IV).

(v) *Artificial Donor Insemination*: This group included 19 conceptions and pregnancy complication in the form of abortion was recorded in 5 subjects (26.32%).

(vi) *Miscellaneous*: Of the 3 subjects conceiving following resection of vaginal septum one had an IUD, and among the 2 subjects treated for Asherman's syndrome one had an IUD.

The different complications encountered in the 6th groups are documented in Table V. Oligospermia treated couples have recorded the minimum number of complications and that two of the less dangerous types. Whereas AID recorded the highest incidence of pregnancy complications spontaneous conceptions following HSG/Laparoscopy, and pelvic infertility surgeries recorded more dangerous complications such as ectopic tubal gestation. As could be expected, multiple gestations were encountered exclusively in the ovulation induction group. Fetal anomalies were also exclusively recorded in the subjects undergoing induction of ovulation. In this series of 349 pregnancies no gestational trophoblastic disease was encountered.

Ectopic Gestation: Ectopic tubal gestation was encountered in 5 subjects, giving an overall incidence of 1.43%. Four of these had conceived spontaneously following laparoscopy or HSG evaluation (3 following laparoscopy and 1 following HSG). The 5th patient was among the 12 subjects who conceived following utero-tubal implantation.

TABLE II
Conceptions Following Induction of Ovulation
(Total pregnancies: 100)

Ovulogene	Total pregnancies	Abortions	Ectopic	Multiple Preg.	Fetal anomaly	I.U.D.	IUGR
Clomiphene Citrate	72	6 (8.33%)	nil	2 (2.78%)	1 (1.39%)	1 (1.39%)	1 (1.39%)
Bromocriptine	19	2 (10. 52%)	nil	nil	1 (5.26%)	nil	nil
hMG/hCG	6	2 (33.33%)	nil	nil	nil	nil	nil
DEX	2	nil	nil	nil	nil	nil	nil
Total	100	10 (10.00%)	nil	2 (2.00%)	2 (2.00%)	1 (1.00%)	1 (1.00%)

TABLE III
Conceptions Following Pelvic Infertility Surgery
(Total pregnancies: 67)

Pelvic surgery	Total pregnancies	Abortions No. %	Ectopic No. %	N.N.D. No. %	Total complications No. %
Endometriosis	40	4 (10.00)	nil	1 (2.50)	5 (12.50)
Utero-tubal implantation	12	3 (25.00)	1 (8.33)	nil	4 (33.33)
Myomectomy	9	2 (22.22)	nil	nil	2 (22.22)
Operative laparoscopy	3	nil	nil	nil	nil
Pelvic adhesiolysis	3	1 (33.33)	nil	nil	1 (33.33)
Total	67	10 (14.93)	1 (1.49)	1 (1.49)	12 (17.91)

TABLE IV
Conceptions Following Treatment of Oligospermia
(Total conceptions: 37)

Treatment of oligospermia	Total pregnancies	Total abortions	Percentage
Human Chorionic Gonadotropin	11	1	9.09
Clomiphene citrate	12	nil	nil
Varicocele Ligation	9	1	11.11
Human Menopausal Gonadotropin and Human Chorionic Gonadotropin	5	nil	nil
Total:	37	2	5.41

TABLE V
Pregnancy Complications in Different Categories of Infertility Subjects

Fertility disorder/ management	Abortions No. %	Ectopic No. %	Fetal anomaly No. %	Twins No. %	Total No. %
Ovulation induction:					
Clomiphene (72)	6 (8.33)	nil	1 (1.39)	2 (2.78)	9 (12.5)
Brom (19)	2 (10.52)	nil	1 (5.26)	nil	3 (15.79)
hMG and hCG (6)	2 (33.33)	nil	nil	nil	2 (33.33)
Pelvic Surgery:					
Endometriosis (40)	4 (10.00)	nil	nil	nil	4 (10.00)
Tubal implantation (12)	3 (25.00)	1 (8.33)	nil	nil	4 (33.33)
Myomectomy (9)	2 (22.22)	nil	nil	nil	2 (22.22)
Unexplained Infertility:					
Laparoscopy (42)	4 (9.52)	3 (7.14)	nil	nil	7 (16.67)
H.S.G. (26)	2 (7.69)	1 (3.85)	nil	nil	3 (11.54)
Clinical (52)	7 (13.46)	nil	nil	nil	7 (13.46)
Oligospermia (37)	2 (5.41)	nil	nil	nil	2 (5.41)
A.I.D. (19)	5 (26.32)	nil	nil	nil	5 (26.52)

Abortions: While the overall incidence of abortion in the 349 subjects was 11.46%, the highest incidence of 26.32% was recorded in the AID group, and lowest (5.41%) in oligospermia group. The other groups recorded an incidence ranging from 10% (ovulation induction) to 14.93% (Pelvic surgery).

Multiple pregnancy and fetal anomalies: These two complications were exclusively seen in subjects undergoing induction of ovulation. There were 2 sets of twin gestations, both following clomiphene therapy. Of the 2 fetal anomalies, 1 was anencephaly in the clomiphene treated group, and the other congenital heart disease (VSD) in the bromocriptine treated group.

Discussion

Certain interesting and important observations have been made by studying the pregnancy outcome in the 349 subjects who had conceived following various forms of infertility evaluations and treat-

ment. The observations seem to have some prospective value and could offer some guidance in prophylaxis against certain complications, and in being more alert at detecting some complications such as ectopic gestation at the earliest.

Evidently, the overall incidence of pregnancy complications (16.33%) is not higher than that in the general population. However, important complications such as ectopic gestation, fetal anomalies and multiple pregnancy were recorded in higher proportion when compared to the general incidence. If pregnancy surveillance is instituted from the time of missed period, these complications could be promptly diagnosed, and optimally managed with minimal maternal and perinatal morbidity. Hence the compelling need for pregnancy monitoring in infertile subjects from the time of missed periods by employing ultrasonography, and beta hCG estimation (if available). In subjects destined to abort during early pregnancy ultrasonography optimally diagnoses the pregnancy complications such as blighted ovum or missed abortion and facilitates early termination of pregnancy and avoids indefinite delay. Moreover, early pregnancy sonography potisively assures a favourable outcome for the pregnancy in more than 95% if an intra-uterine gestation sac is imaged with a live fetus, and this is possible as early as 7 to 8 weeks from the last normal menstrual date. (Jouppila *et al*, 1980, and Romero *et al*, 1984).

Ectopic tubal gestation is encountered more frequently (1.43%), and is confined either to subjects in whom the infertility is unexplained and conception spontaneously follows HSG or laparotomy evaluation, or in subjects undergoing pelvic infertility surgeries. If tubal dysfunction is accepted as the main etiological factor for ectopic gestation then it is understandable why ectopic gestation is seen only in these two groups. Even in those treated by pelvic infertility surgery only the group undergoing tubal implantation was found to be at high risk for ectopic gestation, and those operated for endometriosis did not develop ectopic gestation. This could be because subjects suffering from endometriosis have no tubal luminal pathology. The risk is certainly high when the tubal luminal reconstruction is involved or luminal pathology is existing. Perhaps, infertile subjects with regular cycles and with no explainable cause detected at HSG/laparoscopy are suffering from minimal tubal luminal pathology, and this explains why ectopic gestation is more common in this group. Subjects operated for tubal luminal pathology and those of 'unexplained infertility' should have vigilant early pregnancy surveillance to exclude ectopic gestation.

Ectopic gestation was not encountered in anovulatory subjects and in subjects treated for male fertility disorders. Hence it is reasonable to believe that tubal factor is not a concern in these subjects. Moreover, our earlier laparoscopic study of anovulatory subjects have demonstrated a negligible incidence of pelvic factor in them (Rajan, 1986). Hence we believe that a prior evaluation for tubo-peritoneal factor is quite unnecessary for induction of ovulation, AID or treatment of oligospermia. The very high fertility rate of 73% for ovulation induction with clomiphene citrate and hCG, without a prior pelvic evaluation, also supports this stand (Rajan, 1986). It should be rightly pointed out that rigorous and elaborate early pregnancy surveillance is unnecessary for subjects conceiving follow-

ing ovulation induction, AID and treatment of oligospermia, because ectopic gestation is not usually encountered.

Fetal anomaly as a complication was encountered only in those undergoing ovulation induction. This cautions us against the unindicated and empirical use of ovulation inducing drugs in infertile subjects, and also against irrational hike in dosage regimen.

Another exciting observation is the lowest pregnancy complication rate of 5.41% in couples treated for oligospermia. Correction of male fertility disorder is difficult and is attended with poor pregnancy rate, this study proves that the pregnancy outcome in those few subjects who achieve a conception is excellent. The inference is that male partner does not in general contribute to adverse pregnancy outcome and abnormal pregnancies, and the poor quality sperm of the subfertile male quite often fails to fertilise the ovum, but if conception occurs it is usually achieved through a good quality sperm with normal chromosomal complements. In this context it is prudent to review the pregnancy outcome for subjects undergoing AID. This group has recorded the highest incidence of 26.32% pregnancy complications and all were in the form of abortions. Since male factor has been proved to be an unusual causative factor for a pathological pregnancy, the high incidence of abortions in AID subjects should be explained by improper collection and handling of semen sample. By employing fresh semen sample for AID the pregnancy complications could be minimised.

References

1. Jouppila, P., Huhtaniemi, I. and Tapanainan,: J. Obstet. Gynec. **55**: 42, 1980.
2. Rajan, R. and Vasantha Rajan: J. Obstet. Gynec. India, **36**: 749, 1986.
3. Rajan, R.: 'Operative Laparoscopy for Minimal to mild endometriosis in Infertility', paper presented before 2nd National Congress on Gynaecological Endoscopy, Manipal, 27th and 28th September, 1986.
4. Rajan, R.: Special Lecture on 'Oligospermia', 30th All India Obstet. Gynaec. Congress, Ahemadabad, 28th-30th December, 1986.
5. Rajan, R. and Vasantha Rajan: J. Obstet. Gynec. India, **37**: 1987.
6. Romero, R., Jeanty, P. and Hobbins: Clin. Obstet. Gynec. **27**: 286, 1984.