# MULTICENTRE CASE-CONTROL STUDY OF ECTOPIC PREGNANCY IN INDIA

ICMR Task Force Project


## SUMMARY

**In a multicentric case control study of ectopic pregnancy, 871 ectopic cases were compared with equal number of pregnant controls matched for age, parity and education during a period of one year (Feb. 1987 - Jan. 1988).**

**The data pooled from 32 hospitals indicated an incidence of ectopic pregnancies as 3.12 per 1000 pregnancies or 3.86 per 1000 reported live births. The risk of ectopic abortions (RR 1.8). Women who had history of ectopic pregnancy in the past were at 5 times the risk of developing another ectopic when compared to those with no such history (RR 4.8).**

**Other risk factors observed were tubal surgery including tubal sterilization, D&C and ovarian surgery.**

**A past history of PID had six fold increased risk of ectopic pregnancy (RR 6.4) as compared to women who never had PID.**

**The users (past & current) of contraceptives either IUD or oral pills were not associated with increased risk of ectopic pregnancy.**


## *Introduction*

Ectopic pregnancy occurs when a fertilized egg implants outside the uterus. It happens, either because the mechanism that transports the egg through the fallopian tube to the uterus malfunctions or because the tubal pathway is obstructed. A tubal pregnancy which is the commonest type of ectopic pregnancy is a serious condition that can result in tubal rupture and internal haemorrhage.

National level population based data in India is lacking both in respect to the incidence of ectopic pregnancy and the associated risk factors. Last five years statistics from few hospitals have shown a steady increase in the incidence of ectopic pregnancies. It has been suggested that the rise in the incidence may be due to changes in underlying risk factors such as pelvic inflammatory disease and sexually transmitted diseases, prior ectopic pregnancy and tubal surgery or the use of fertility regulation methods such as intrauterine devices (IUDs), sterilization and abortion (Rubin et al. 1983 and

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*Participating investigators and Co-ordinating Unit listed at the end of paper.*

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Tuomivaara, L. and Kauppila 1988).

The Indian Council of Medical Research has conducted a multicentric matched case control study, with an aim to determine the etiology of ectopic pregnancy and its incidence in hospital admissions during pregnancy and also to determine whether the use of contraceptive is associated with an increased or decreased risk of ectopic gestation and whether infective conditions are associated with an increase or decrease in ectopic pregnancy.

### *Study Design and Methodology*

The net-work of 32 Human Reproduction Research Centres (HRRCs) of the ICMR participated in the study using uniform criteria for selection/identification of cases and controls, recording data in pretested and pre-coded, proformae. The data handling and analysis was taken up by the co-ordinating unit located in the ICMR Headquarters. The admissions/referrals to gynaecology and obstetric departments were reviewed daily to identify the ectopic cases during one year period i.e. from Feb., 1987 - Jan. 1988. For each case of ectopic pregnancy, a pregnant control was identified matched with the case for age, parity and education, from women attending ante-natal clinic.

Diagnosis of 'Ectopic' was arrived at by performing examination and procedures varying from culdocentesis, laparoscopy, ultrasonography depending upon the facilities available and the subjects' clinical condition. Both the ectopic case and pregnant control were interviewed to collect the requisite information. Data on demographic profile, obstetric and gynaecological profile, surgical and medical history was collected. Past history of PID/STD, and contraceptive use was also recorded.

In cases of ectopic pregnancy details of diagnostic procedure, site and side of ectopic pregnancy and management were noted.

To obtain denominator statistics on pregnancies, hospital admissions were reviewed which include admission for ectopic pregnancies, legally induced abortions, still births and live births.

Maximum likelihood estimates of relative risk was calculated for each individual factor and MC Nemar's test for equality of proportion in matched samples was used for test of significance.

### *Observation*

A total of 871 ectopic cases and their matched pregnant controls were enrolled during a period of one year. The mean age of the ectopic case was 28.0 years and mean parity was 2.1. The pregnant controls matched well with the cases with respect to age, parity and education. Around 47% cases had education above primary level. (Table I).

**TABLE - I**
**DEMOGRAPHIC PROFILE**

| | Case | Pregnant Control |
|---|---|---|
| Age in years (Mean ± S.D) | 28.0 ± 4.9 | 27.6 ± 4.7 |
| Gravida (Meant ± S.D) | 2.1 ± 1.8 | 2.0 ± 1.7 |
| Education upto Primary (%) | 53.2 | 52.1 |
| Education above Primary (%) | 46.8 | 47.9 |
| Total No. | 871 | 871 |

### *Incidence of Ectopic*

The incidence of ectopic pregnancy in the hospital reported pregnancies (which include live births, still births, ectopic pregnancies and induced abortions) was

3.12/1000 pregnancies or 3.86/1000 live births.

### *Location of Implantation Site*

Occurence of ectopic was almost equal on both sides (Right side 455 and left side 411 cases). Of the remaining 5 subjects, in one woman, the implantation was detected in both the tubes and in 4 women, the side could not be identified due to dense adhesions.

The actual site of ectopic could be identified in only 839 subjects. Fallopian tube specially the middle and outer third of the tube was the most common site of implantation (93.9%). The other sites included cornual and ovary; abdominal, broad ligament and rudimentary horn of uterus were rare sites where embedding occured. In only 32 cases the implantation site could not be identified due to dense adhesions (Table II).

### *Management*

The operative procedure undertaken depends on the site of the ectopic and the extent of damage due to the ectopic. In view of tubular ectopic being the commonest, salpingectomy or salpingo-oophrectomy was the most frequent surgery performed (90.48).

Table III shows the details of surgery performed. Most subjects had to undergo a major surgery requiring average hospital stay of seven days. In 37.6% women hospital stay was prolonged beyond 10 days. There was one woman who died following surgery. The woman, 27 years of age, second gravida was admitted with history of 45 days amenorrhoea. On examination she was severely anaemic (HB 4gm) and was in shock; after resucitation with I.V. fludis and blood transfusion, laparotomy was performed. There was massive haemoperitoneum. Right ampullary region was ruptured and actively bleeding. Right sided total salpingectomy was performed. She expired 20 hours after operation due to Mendelson's syndrome (post-operative respiratory aspiration). Cause

**TABLE II**
**SITE OF ECTOPIC**

| | Site of Ectoic | Number | Percentage |
|---|---|---|---|
| 1. | Tubular<br>Inner Third - 109<br>Middle Third - 279<br>Outer Third - 252<br>Bilateral - 1<br>Tubal Mole - 3<br>Tubal abortion - 71<br>Site not known - 16<br>(Old Tubal Rupture) | 731 | 83.9 |
| 2. | Cornual | 67 | 7.7 |
| 3. | Ovarian | 22 | 2.5 |
| 4. | Other site (abdominal, cervical, broad ligament rudimentary horn etc.) | 19 | 2.2 |
| 5. | Site could not be identified due to adhesions | 32 | 3.7 |
| | Total cases | 871 | 100.0 |

of death reported was Mendelson's syndrome.

***Risk Factors***

Table IV shows the prevalence of previous obstetric history, previous surgery, history of PID, tuberculosis of genital tract and history of contaceptive use in cases and pregnant controls.

When the cases were compared with pregnant controls it was observed that

**TABLE III**
**MANAGEMENT OF CASES & TYPE OF SURGERY**

| Metod | No. of Cases | Percentage |
|---|---|---|
| Type of tubal Surgery performed | | |
| 1. Salpingectomy unilateral/Bilateral Salpingo-oophrectomy | 787 | 90.4 |
| 2. Fimbriectomy | 8 | 0.9 |
| 3. Salpingiostomy/Salpingolysis | 8 | 0.9 |
| 4. Milking of tube for removal of products/Foetus | 45 | 5.1 |
| Other Type of Surgery performed | | |
| 5. Cornual end stitched | 5 | 0.6 |
| 6. Oophrectomy/ovariotomy | 4 | 0.5 |
| 7. Hysterectomy with or without Salpingo-oophrectomy | 14 | 1.6 |
| | 871 | 100.0 |

**TABLE IV**
**PREVALENCE OF RISK FACTORS AMONGST CASES & CONTROLS & RELATIVE RISK**

| Risk Factor | Cases | Pregnant Control | R.R. |
|---|---|---|---|
| A. OBSTETRIC HISTORY | | | |
| Induced abortion | 13.2 | 8.3* | 1.8 |
| Spont. abortion | 13.1 | 10.7 | 1.3 |
| Ectopic Pregnancy | 2.9 | 0.7* | 4.8 |
| B. H/O SURGERY EXCLUDING STERILIZATION | | | |
| Tubal surgery for infertility | 1.4 | 0.3* | 5.5 |
| Salpingectomy | 2.9 | 0.2* | 24.6 |
| D&C (either for abortion or any other reason) | 19.1 | 6.6* | 3.7 |
| Ovarian Surgery | 1.2 | 0.1* | 10.0 |
| Caesarean | 5.6 | 6.2 | 0.9 |
| Any other abdomen surgery | 2.1 | 0.5* | 4.5 |
| C. H/O | | | |
| PID (Symptoms and suggestive of PID) | 10.6 | 2.0* | 6.4 |
| T.B. of genital tract | 2.2 | 0.1* | 19.0 |
| Infertility | 10.0 | 2.3* | 12.0 |
| D. H/O CONTRACEPTIVE USE (Ever user) | | | |
| Sterilization | 12.5 | 0.9* | 15.4 |
| IUD | 9.9 | 9.2 | 1.1 |
| Pill | 3.4 | 3.8 | 0.9 |
| E. CURRENT USER OF CONTRACEPTION | | | |
| Pill | 1.4 | 2.5 | 0.5 |
| IUD | 6.3 | 6.4 | 1.0 |
| | 871 | 871 | |

* Statistically significant difference.

higher proportion of cases had history of induced abortion (13.2%) and ectopic pregnancy (2.9%) as compared to pregnant controls. The risk of ectopic pregnancy is almost double in women who had history of induced abortion (RR 1.8) in comparison to women who never had induced abortion and the risk of ectopic pregnancy is increased almost five folds in women who had history of previous ectopic in comparison to women who never had ectopic pregnancy. The prevalence of spontaneous abortion were similar in cases and pregnant controls.

Other risk factors observed were tubal surgery including tubal sterilization, D & C and ovarian surgery.

A past history of PID had six fold increased risk of ectopic pregnancy (RR 6.4) as compared to woman who never had PID. The woman who had positive history of tuberculosis of genital tract had 19 fold increased risk of getting ectopic pregnancy and women who had treatment for infertility had 12 fold increrased risk of getting ectopic pregnancy as compared to woman who never had these problems.

The users (past and current) of contraceptives either IUD or oral pills were not associated with increased risk of ectopic pregnancy.

***Discussion***

The objective of study was to determine the etiology of ectopic pregnancy and its incidence in hospital admissions during pregnancy; also to determine whether the use of contraceptive is associated with an increase or decrease in ectopic pregnancy.

The incidence of ectopic in this study was observed to be 3.12 per 1000 pregnancies registered in the hospitals which include live births, still births, induced abortions and ectopic pregnancies or 3.86 per 1000 live births resulting in ratio of 1:250. The incidence of ectopic reported by other authors in India 1:266 (Pendse 1981) and D'Mello 1:214 (1988).

Majority of the cases were in the age group of 25 to 35 years. Approximately 20% of ectopic cases were Nulliparous women. Out of 871 ectopic cases. 12.4 percent of the ectopic occurred at the sites other than fallopian tube and in 3.7 percent of cases site of implantation could not be identified.

It was observed that H/O induced abortion (RR.1.8) and ectopic pregnancy (RR 4.8) was associated with increased risk of ectopic when compared with pregnant controls which is in confirmity with the findings of Panayotou et al (1982) and Chung et al (1982).

In the present study prevalence of tubal surgery for infertility, salpingectomy, dilatation and curettage (D&C) for abortion or other reasons and ovarian surgery in women had high relative risk when cases are compared with pregnant controls.

Although we do not have information on life style or sexual activity (STD), the relative risk was significantly increased in women who had symptoms suggestive of PID (RR 6.4) which is in conformity with prospective studies in Sweden (Westrom et al 1981).

The women who had history of infertility have higher chance of ectopic pregnancy.

Pregnancy rates following sterilization is low, but if conception occurs it is more likely to ectopic due to partial tubal occlusion. It is evident from the observa-

tion that the prevalence of sterilization was significantly higher in ectopic cases when compared with pregnant controls (RR 15.4)

Ory (1981) reported that past IUD use was associated with grater risk of ectopic pregnancy than current IUD use. However our data did not suggest that IUD use prior to conception significantly affects the risk of ectopic pregnancy. The multinational, multi-centre case control study conducted by WHO (1985) in both developed and developing countries showed that the relative risk was less than 1.0. The current IUD users are not at any high risks of ectopic pregnancy than non-contraceptors.

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