



**ORIGINAL RESEARCH PAPER**

**Obstetrics & Gynecology**

**“HOSPITAL BASED CASE CONTROL STUDY OF RISK FACTORS ASSOCIATED WITH ECTOPIC PREGNANCY IN OUR SOCIODEMOGRAPHIC SETUP”**

**KEY WORDS:**

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**ABSTRACT**

**Background:** Ectopic pregnancy is assuming greater importance because of its increasing incidence and its impact on woman's fertility.

**AIM:** To assess the frequency and to determine an association between the studied risk factors and ectopic pregnancy.

**Materials and METHODS:** A retrospective case-control study was conducted for the role of several risk factors in the occurrence of ectopic pregnancy in department of obstetrics and Gynecology, LD Hospital. A total of 110 cases and 110 controls were compared for socio demographic characteristics, cigarette smoking, obstetrical and gynecological history, PID, past exposure to Chlamydia, surgical histories, the presence of assisted conception and contraceptive usage.

**RESULTS:** In present study the main risk factors for ectopic pregnancy were history of Tuberculosis (OR=12.11), history of infertility (p=0.001), abortions (p=0.01) and a history of Prior ectopic pregnancy (OR=8.549). Other risk factors found to be associated with an increased risk for ectopic pregnancy were PID / Chlamydia infection (OR=5.63), endometriosis (5.40), induced conception cycle (OR=3.063), intrauterine device usage (OR=3.55), prior Caesarean section (OR=2.83) and Appendectomy (OR=2.25). On the contrary, barrier methods (OR=0.28) and oral contraceptive use (OR=0.28) were protective from ectopic pregnancy.

**CONCLUSIONS:** Pelvic infection particularly TB was found to be a major etiological factor for ectopic pregnancy in our setup. Furthermore, other factors found to be associated with ectopic pregnancy, such as prior ectopic pregnancy and infertility history may be the result of a previous pelvic infection that caused tubal sequele. Thus these factors are potential targets for intervention and modification. Further, patients with previous abortions, pelvic surgeries, induced conception cycle and IUCD users should be counseled about the possible risk when they conceive.

**INTRODUCTION:**

An ectopic pregnancy or eccysis derived from a Greek word ektopos, out of place, is one in which the fertilized ovum becomes implanted in the site other than the normal uterine cavity<sup>1,2</sup>. It is the result of a flaw in human reproductive physiology that allows the conceptus to implant outside the normal endometrial cavity which without timely diagnosis and treatment becomes a life threatening situation<sup>3</sup>. Apart from being a form of reproductive failure in the index pregnancy of affected women, such women have 7 – 15% chances of recurrence and only 40 – 60% chances of conceiving after surgery<sup>4</sup>.

Worldwide, the incidence of ectopic pregnancy is increasing .A number of reasons at least partially explain the increased rate of ectopic pregnancy. Some of these include increasing prevalence of STDs, identification through earlier diagnosis, popularity of contraception that predisposes pregnancy failure be ectopic, tubal sterilisation techniques that with contraceptive failure increases the likelihood of ectopic pregnancy, Assisted reproductive technology and tubal surgery<sup>1,4</sup>.

It is believed that 25 – 50% of patients with ectopic pregnancy have predisposing risk factors<sup>5</sup>. Though, several studies assessing the risk factors of ectopic pregnancy have been published from both developed and developing countries<sup>6</sup>. Risk factors and thus the incidence of the condition vary from country to country and within the same geographical region<sup>7</sup>. Since women in our setup too have different cultural, religious, sociodemographic, sexual behavior and beliefs and contraceptive practices, therefore the risk factors and thus the incidence of ectopic pregnancy may differ.

**MATERIAL AND METHODS:**

This study was conducted at Government Lalla Ded Hospital, associated with Government Medical College, Srinagar and was supported by the Department of Microbiology for investigation purpose.

This study was conducted for a term of 18 months, where 110 cases and 110 controls were studied. Ectopic pregnancy was

confirmed in hospital by beta-HCG levels, transvaginal sonography and laparoscopy / laprotomy and an equal proportion of non-ectopic pregnancies were taken as controls i.e. women who delivered a single term live born neonate by vaginal or abdominal route via a uncomplicated pregnancy after index case of ectopic pregnancy in the same centre after matching some appropriate socioeconomic and sociodemographic characteristics. A detailed history was collected from cases and controls with the help of proforma after taking written informed consent. The history included age, residence, education, occupation, socioeconomic status (modified B G Prasad scale), parity, prior abortions, prior ectopic pregnancies, post abortion and puerperal febrile illness, tubal corrective surgeries, tubal sterilization, intrauterine contraceptive device (IUCD) use, oral contraceptive pills, post coital pills, documented tubal pathology, history of infertility, history of assisted reproductive techniques, history of pelvic inflammatory disease, history suggestive of endometriosis, history of sexual transmitted diseases and prior caesarean delivery.

An association between exposure of Chlamydia trachomatis and ectopic pregnancy was determined by testing IgG antibodies to Chlamydia trachomatis in cases and controls by using ELISA kits.

**RESULTS:**

**Results and observations in this study are as depicted in table 1**

**TABLE 1**

Risk Factors	%age of Cases	%age of Controls	Results
Age 30 years	56.4%	36.3%	P=0.012
Low SES	57.2%	8.1%	P<0.001
Smoking	4.5%	1.8%	OR=2.57
Parity1	65.6%	51.8%	P=0.008
Abortions	22.7%	10%	P=0.01
PID	20%	8.2%	OR=2.806
TB	10%	0.9%	OR=12.11

Chlamydia	13.6%	2.7%	OR=5.63
Endometriosis	9.1%	1.8%	P=0.038
Infertility	18.2%	2.7%	P<0.001
OI	12.7%	4.5%	OR=3.063
Barrier Method	5.5%	17.3%	OR=0.28
Post Coital Pill	2.7%	0%	P=0.245
OCP	4.5%	14.5%	OR=0.28
IUCD	11.8%	3.6%	OR=3.55
LSCS	18.2%	7.3%	OR=3.55
Appendectomy	20%	10%	OR=2.25
Myomectomy	3.6%	0.9%	OR=4.113
Ovarian Surgery	5.5%	0%	OR=4.283
Previous Ectopic	7.3%	0.9%	OR=8.549

- The risk of ectopic pregnancy increased with age and it remained statistically significant (p=0.012).
- Ectopic pregnancy occurred more in lower socioeconomic status as compared to controls. (p<0.001).
- Smoking increases risk of ectopic pregnancy with OR 2.57 (95% CI= 0.49, 13.55).
- 20 cases (18.2%) and 10 controls (9.1%) had prior one abortion (spontaneous/induced) whereas 5 cases (4.5%) and 1 control (0.9%) had prior two abortions. This association was found statistically significant (p=.01).
- Out of 110 cases, majority (52.7%) had prior one delivery whereas majorities (46.2%) of control were primigravida. The association was found statistically significant (p =0.008).
- 22 (20%) of cases and 9 (8.2%) of controls had evidence of PID, OR was found to be 2.806(95% CI= 1.23, 6.41).
- Among cases 11 (10%) had history of TB and among controls 1 (0.9%) one had such history. OR was 12.11 (95% CI= 1.54, 95.56).
- IgG anti Chlamydia antibody testing using ELISA kits was positive in 15 cases (13.6%) and 3 controls (2.7%). OR was 5.63 (95% CI 1.58, 20.06).
- 10 cases (9.1%) had evidence of endometriosis and 2 controls (1.8%) had evidence of endometriosis. OR was found to be 5.40 (95%CI 1.5, 25.26).
- Of 110 cases studied, 12 cases (10.9%) had history of primary infertility and 8 cases (7.3%) had history of secondary infertility, whereas of 110 controls studies, only 2 cases had history of primary infertility and only one control had history of secondary infertility. This association was statistically found to be significant (p value <0.001).
- 12.7% of cases and 4.5% of controls conceived after ovulation induction in present pregnancy with or of 3.063 (95%CI=1.06,8.82).
- 6 cases (5.5%) had history of use of barrier contraception whereas 19 controls (17.3%) had history of use of Barrier contraception. OR was 0.28 (CI 0.11, 0.72)
- Only 3 cases gave history of intake of levonorgestrel in index pregnancy whereas none of the controls gave such a history. OR was 7.195.
- 5 cases (4.5%) had history of OCP use whereas of 110 controls studied, 16 controls (14.5%) had similar history. As per this study the rate of ectopic pregnancy among pill users was lower than non users with OR=0.28 (CI 0.10, 0.79).
- Pelvic surgeries were found to be associated with ectopic pregnancy. Of 110 cases, 20 cases (18.2%) had previous history of LSCS and of 110 controls, 8 controls (7.3%) had previous history of LSCS. OR was 2.83 (CI 1.19, 6.75). with history of Appendectomy or was 2.25(95%CI 1.03, 4.90), history of myomectomy or was 4.113(95%CI=0.45, 37.42) and history of ovarian Surgery OR was 2.019 (95%CI 0.18, 0.60).
- In this study 8 (7.3%) cases and 1 (0.9%) controls had previous history of ectopic pregnancies. OR was 8.549 (CI 1.05, 69.59).

**DISCUSSION:**

Many risk factors have been identified and implicated in the increasing incidence of ectopic pregnancy.<sup>3,8,9</sup>In our study, the risk of ectopic pregnancy increased with increasing age (p=0.012). Bouyer Jetal<sup>6</sup> and Sivalingam VNetal<sup>10</sup> in their study have also found this association. Ectopic pregnancy occurred more in lower socioeconomic status in present study, similar results were found

by authors like Yuk J Setal<sup>11</sup> and Aboyeji AP<sup>12</sup>. Smoking appeared to be a risk factor in this study, with authors like Handler Aetal<sup>13</sup> and Bastianelli Catel<sup>14</sup> reporting similar results.

Our study depicted statistically significant association between history of abortions and ectopic pregnancy. Similar association was reported by Tharoux-Beneux Cetal<sup>15</sup> and Bouyer J et al<sup>6</sup> with (p ≤0.001) in both studies. The risk of ectopic pregnancy increased with increasing parity. Authors like Aziz Setal (2011)<sup>16</sup> and Al Daheen G<sup>17</sup> having similar results. In our study endometriosis was found to have an association with EP, similar to observations made by studies like Jobspira Netal<sup>18</sup> and Hunter RHF<sup>19</sup>.

PID was seen to be associated with ectopic pregnancy. Mol B W Jetal<sup>20</sup> and Bouyer Jetal<sup>6</sup> also observed the same. TB was found in 10% of cases compared to only 0.9% of controls with OR of 12.11. Ghosh Ketal<sup>21</sup> and Shah Netal<sup>22</sup> have also reported association of ectopic pregnancies with tuberculosis. 13.6% of cases and 2.7% of controls were positive for Chlamydia IgG antibodies. These observations were comparable to the observations made by Mol B.W.Jetal<sup>20</sup> and Agholor Ketal<sup>23</sup>. Infertility and ovulation induction were found to be associated with EP. Studies by Malak Metal<sup>24</sup> and Ankum W Metal<sup>25</sup> have also found infertility as a risk factor for Ectopic pregnancy. Authors like Karaer A et al<sup>26</sup> and Fernandez H et al<sup>27</sup> have mentioned associated of EP and ovulation induction .

Certain types of contraception have been implicated as a risk for occurrence of ectopic pregnancy. In our study it was found that contraceptive methods like barrier and ocp lowered the risk. Anorlu RI et al<sup>7</sup> and Karaer A et al<sup>26</sup> in their study found that Barrier methods were protective from Ectopic Pregnancy. Bouyer J et al<sup>6</sup> and Mol BWJ et al<sup>28</sup> in the study reported that the Previous use of oral contraception was associated with a decreased risk of ectopic pregnancy. Contraceptive methods like pop and iucd were found to be a risk for ectopic pregnancy with OR for pop as 7.19 and 3.55 for iucd usage. Basu A et al<sup>29</sup> in a case presentation mentioned that a woman presented with an ectopic pregnancy after use of levonelle-2 (a postcoital contraception) in absence of other predisposing risk factors. Jain S H et al<sup>30</sup> found that hormonal emergency contraceptive pills failure rate is high when used in periovulatory period with increased chance of ectopic pregnancy. Anorlu RI et al<sup>7</sup> and Karaer A et al<sup>26</sup> reported that use of IUCD increased the risk of ectopic pregnancy.

Previous history of ectopic pregnancy was found to a significant risk factor of ectopic pregnancy. Authors like Ankum WH et al<sup>25</sup> and Karnus L Letal<sup>31</sup> have also reported similar association. History of pelvic surgeries like lscs, Appendectomy, Myomectomy and Ovarian Cystectomy were evaluated and found to be associated with ectopic pregnancy. Authors like Karaer A et al<sup>26</sup>, Bastianelli Cetal<sup>14</sup>, Coste Jetal<sup>32</sup>, Michalas Setal<sup>33</sup>, Malak Metal<sup>24</sup>, Strandell Aetal<sup>34</sup> and Brodowska Aetal<sup>35</sup> in their study have found similar results.

**RECOMMENDATIONS:**

After reviewing literature and our results following strategies be recommended.

- Screening and early treatment for TB in reproductive age group should be done so that tubal damage can be prevented. Similarly screening and treatment for Chlamydia infection in reproductive age group is an important measure to prevent tubal damage.
- Women with higher parity and those in lower socioeconomic class should be in target group while counseling for risk of ectopic pregnancy in their future pregnancy and stressing the need for improving their socioeconomic status to reduce the risk.
- Women with past history of ectopic pregnancy should be kept under surveillance and counseled adequately. So that they are picked up early and managed accordingly. Thus reducing their morbidity and mortality.
- Importance of effective contraception needs to be stressed on, so that rate of abortions can be reduced and therefore reducing the risk of ectopic pregnancy. Implementation of the

concept of safe abortion is another way of preventing risk of ectopic pregnancy.

- One of the preventive measures to decrease the risk of ectopic pregnancy is to properly counsel the patients for the future risk before on demand LSCS.
- Further, patients with risk factors like pelvic surgeries (especially appendectomy, ovarian surgery, myomectomy etc), Endometriosis, induced conception cycle, Post coital pill and IUCD users should be counseled about the possible risk of ectopic pregnancy once they conceive. So that they are kept under surveillance for early detection.

#### CONCLUSION:

- PID particularly TB and Chlamydia are major etiological factors for ectopic pregnancy in our setup. Furthermore, prior ectopic pregnancy and infertility history may be the result of a Previous PID that might have caused tubal sequele.
- Advancing maternal age and low socioeconomic status are risk factor for ectopic pregnancy possibly due to increased chances of exposure to STDs and PID.
- History of previous ectopic pregnancy has a strong association with next pregnancy being ectopic pregnancy.
- Previous history of abortions either spontaneous or induced is strongly incriminated as an etiological risk for ectopic pregnancy. In our study none of the cases or controls had history of multisexuality, which constitutes an important risk factor in western countries.

Due to increasing trend towards LSCS, risk of ectopic pregnancy is increasing. Our study also depicted an important association between pelvic surgeries (especially appendectomy, ovarian surgery, myomectomy etc), Endometriosis, induced conception cycle, Post coital pill and IUCD users, and ectopic pregnancy.

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