

Original Article

Risk Factors for Ectopic Pregnancy: A Case-Control Study in a Teaching Hospital of West Bengal

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ABSTRACT

Background: Ectopic pregnancy occurs when a fertilized ovum implants other than the uterine cavity. It is the most important cause of maternal mortality and morbidity in the first trimester. For early and more accurate diagnosis of ectopic pregnancy in the women who are at higher risk, knowledge of the associated risk factors is immensely helpful.

Material & Methods: In this case-control study 74 cases with diagnosed ectopic pregnancy and 74 controls with intra-uterine pregnancy, were selected from the obstetrics emergency and outdoor over a period of one year. They were interviewed with a standard uniform questionnaire about their different socio-economic structures, cultural practices, life style, habits, diseases and important medical or surgical co-morbidities. The data gathered, then entered in MS Excel 2016, and transferred to IBM SPSS software version 22.0.

Results: After collecting data, we analysed various factors that may have significant effects on ectopic pregnancy. Out of all the variables, we found 4 variables which were statistically significant. Addiction (p-value .001), multiple sexual partner (p-value .008), previous ectopic pregnancy (p-value .029), and PID (p-value .002) were statistically significant. Other variable we found were in concurrence with previous studies though statistically insignificant.

Conclusion: Ectopic pregnancy is one of the major reasons of mortality and morbidity in first trimester pregnancy. A highly suspicious mind, proper clinical knowledge and idea about the local risk factors will be helpful to successfully manage the grave health problem.

Key words: case-control study, ectopic pregnancy, intra-uterine pregnancy, risk factors

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Introduction

Ectopic means which is not in place where it should be. Likewise, an ectopic pregnancy (EP) occurs when a fertilized ovum implants other than the uterine cavity.¹ It is the most important cause of maternal mortality and morbidity in the first trimester.² For early and more accurate diagnosis of ectopic pregnancy in the women who are at higher risk, a knowledge of the associated risk factors is immensely helpful.³ Most risk factors are associated with risks of prior damage to the Fallopian tube. These factors include any previous pelvic or abdominal surgery, and pelvic infection.⁴ Chlamydia trachomatis infection contributed 30-50% of all ectopic pregnancies.⁵ Various factors like previous ectopic pregnancy, smoking, multiple sexual partners, infertility, tubal sterilization, intrauterine devices, documented tubal pathology, tubal corrective surgery, assisted reproductive techniques, PID (Pelvic inflammatory disease), prior abortions, and prior delivery have important role in causing ectopic pregnancy.⁶ Diagnosis and management of ectopic pregnancy is a big challenge to all obstetricians. This is a preventable pathological condition when diagnosed in time. Ultrasound is essential in the evaluation and management of pregnancies of unknown location. Both transabdominal and transvaginal reports should be available, in addition to physical examination, for complete evaluation.⁷ In many occasion, women attend emergency ward in a critical condition which makes it more difficult to manage. Emergency laparotomy along with massive volume transfusion and ICU (Intensive care unit) monitoring become necessary. To avoid this situation, it's better to prevent the ectopic implantation in the first place. About (1-2)% of all naturally conceived pregnancies are found to be ectopic pregnancies. Although, the risk factors have been analysed in various studies, but over the past decades, the overall incidence has increased. The

exact role and strength of these factors may vary over years with our changing habits and life styles. It also may vary with changes of geographical areas, races and cultures. The purpose of this study is to evaluate the changing scenario in the contribution of individual risk factors associated with EP, in a tertiary health centre in West Bengal. An observational case control study is ideal for detecting the local and regional risk factors for ectopic pregnancy and it can provide us prior knowledge about the disease and the possible population that are in risk.

Materials and Methods

This was an analytical epidemiological case-control study conducted at the department of Obstetrics & Gynaecology, College of Medicine & JNM Hospital, WBUHS, Kalyani (COMJNMH) from January 2018 to June 2019. Kalyani is a municipality town in Nadia district of West Bengal. The total population of the town is 100575 as per census 2011 with a population density of 35001. It is situated around 50 km from Kolkata city. This hospital caters its patients from the city and surrounding places of Nadia, North 24 parganas, Hoogly, East Burdwan as well as parts of the neighbouring country like Bangladesh. The patients were recruited from the obs-gynae emergency and indoor. All diagnosed cases of ectopic pregnancy within the study period who could understand the survey questionnaires were included in the study and normal uterine pregnancy that has crossed first trimester were taken as control. Women with any of these: 1. Corpus luteal cyst, 2. Ovarian torsion, 3. PID, 4. Endometriosis 5. Ruptured haemorrhagic cysts were excluded from the study.

Sample size calculation was done basing on assumptions that Odds ratio: 3, Incidence of PID in exposed controls: 15%, Alpha: 5%, Power: 80%. The estimated sample size (number of pairs) was 74, making the total sample size 148. Development and

pre-testing of tools took 15 days of time. A semi-structured predesigned and pretested questionnaire in English was used. It had questions related to Socio-demographic-economic, menstrual history, white discharge, bathing in pond, History of ART (Assisted reproductive techniques), PID, history of trauma over abdomen etc. The questionnaire thus prepared was pre-tested in pregnant women attending the OBGYN OPD of COMJNMH who were not part of the study. Pretesting participants as well as study participants all were surveyed by first author to avoid bias. Data collection was finished in one-year time. Data entry, analysis and report preparation took another 6 months.

Collected data was entered in MS Excel 2016 and then transferred to IBM SPSS® software, version 22.0 (SPSS Inc., Chicago, IL, USA). Student's t-test or Mann-Whitney U-test was used for continuous variables. Pearson's Chi-square test or Fisher's exact test was used for categorical variables. Quantitative variables were expressed as mean \pm standard deviation. Qualitative variables were presented with number and percent. Association between ectopic pregnancy and factors studied will be measured by odds ratio (ORs) and 95% confidence interval (CI) was found out. Logistic regression analysis was done to calculate ORs and 95% CI. Subsequently, multiple logistic regression was used to select independent predictors for ectopic pregnancy. The data were summarized with tables and appropriate diagrams. Two tailed significance tests with p value of less than .05 was considered as statistically significant.

Results

Total 148 including 74 cases and 74 controls were interviewed and various data plotted in charts and tables. Major number of ectopic pregnancy as well as intra uterine pregnancy were found in the age group of 25-29, may be

because of more reproductive activity in this age group. Chances of ectopic pregnancy were found to increase with increment of gravidity with almost 78% of cases where gravidity was two or more. We also tried to find out, if residence had any role on ectopic pregnancy - 51.35% of total cases were from rural areas and 63.51% were home makers. We also found that 17.57% and 6.76% of the cases were regularly taking bath in ponds and rivers respectively. Irregular menstrual cycles were reported by 21.62% of women with ectopic pregnancy and almost 83% of them had pain during different times of their menstrual cycle. Sanitary pads were used by 67.57% while others used unhygienic methods like clothes or clay/ash etc. Thirty-one percent (31%) had no idea about perineal and menstrual hygiene. Almost 47% suffered from white discharge of different duration. Past history of sexually transmitted disease was present in 16.22% cases and 2.7% of them mentioned that their husbands also suffered from the same.

The most significant variable in the socio-economic group was the women with multiple sexual partners. Although only 4.05% of them admitted that they had active multiple sexual partners but the p-value was significant at .008. (Fig. 1)

Another significant risk factor was the addiction habits. 20.3% of the cases had smoking habits, whereas 28.4% and 10.81% had habits of paan and gutkha. The risk factor addiction has p-value of .001 and we found it to be a very significant risk factor. (Fig. 2)

Women who undergone different treatments for infertility did not had much incidence of ectopic pregnancy. We also took history of different methods of contraception they used and almost 56% of them were following different methods in the form of IUCD/POP/OCP/BARRIER/ECP (terms used as a broad spectrum as specific types could not be recalled by the subjects). Tubal

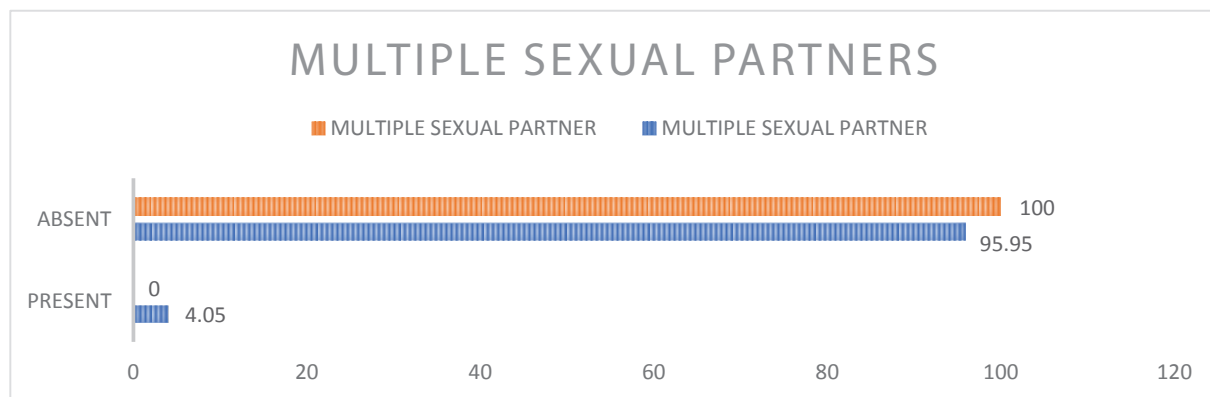


Figure 1: Multiple sexual partners and ectopic pregnancy

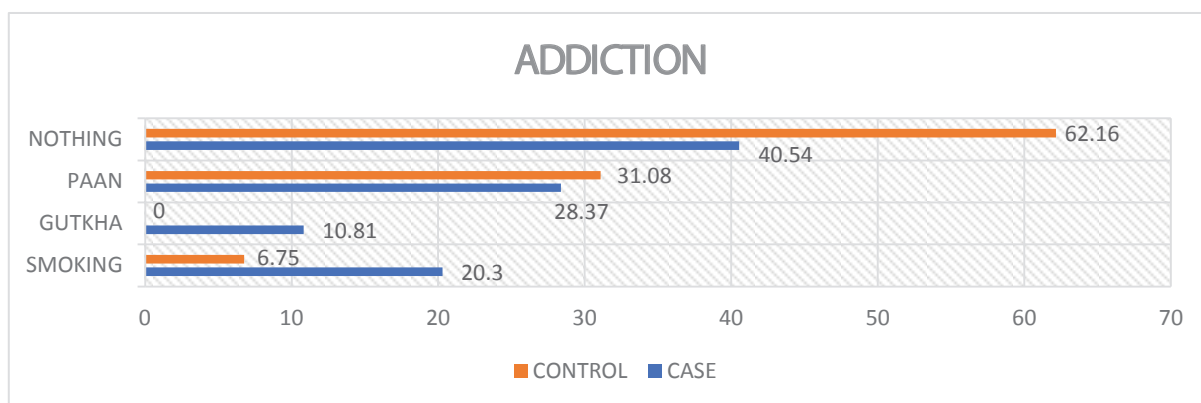


Figure 2: Addiction and ectopic pregnancy

ligation was done in 5.41% cases (2.7% had laparoscopic ligation) and the p-value was .043 which was a significant one. Another risk factor, previous history of ectopic pregnancy was present in 9.46% cases (p value .029, significant). (Fig. 3)

Of all the cases, 29.73% gave history of previous induced abortion from quacks or registered MTP clinics. Around 28% of them had one or more number of abortions. History of endometriosis was present in 5.41% cases; 2.7% & 1.35% had uterine and cervical anomalies respectively.

Significant association of diagnosed pelvic inflammatory diseases in the past was found, 28.37% (p value .001). (Fig. 4) Regarding mode of delivery in the past

- 24.32% cases had previous delivery by caesarean section whereas 8.1% had assisted vaginal delivery. History of previous surgery was present in 6.67% cases.

Discussion

The incidence, epidemiological factors, diagnostic methods have changed significantly over the past decades. Although we did not concentrate on calculating the incidences of ectopic pregnancy, but detecting the risk factors that has some association with higher incidence, will help us to reduce the risk. Presence of various risk factors may strengthen the suspicion, but their absence does not rule out ectopic pregnancy.

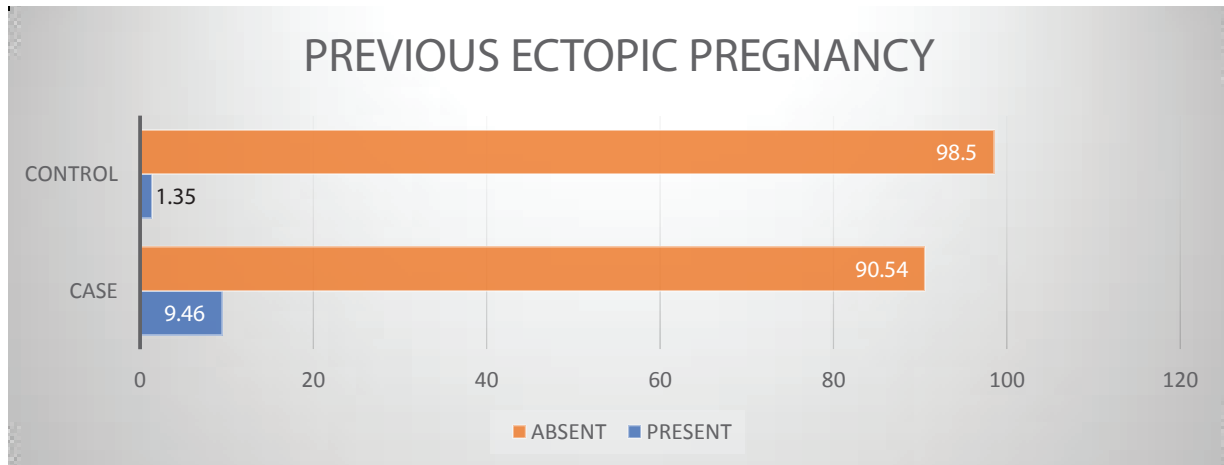


Figure 3: Previous ectopic pregnancy and ectopic pregnancy

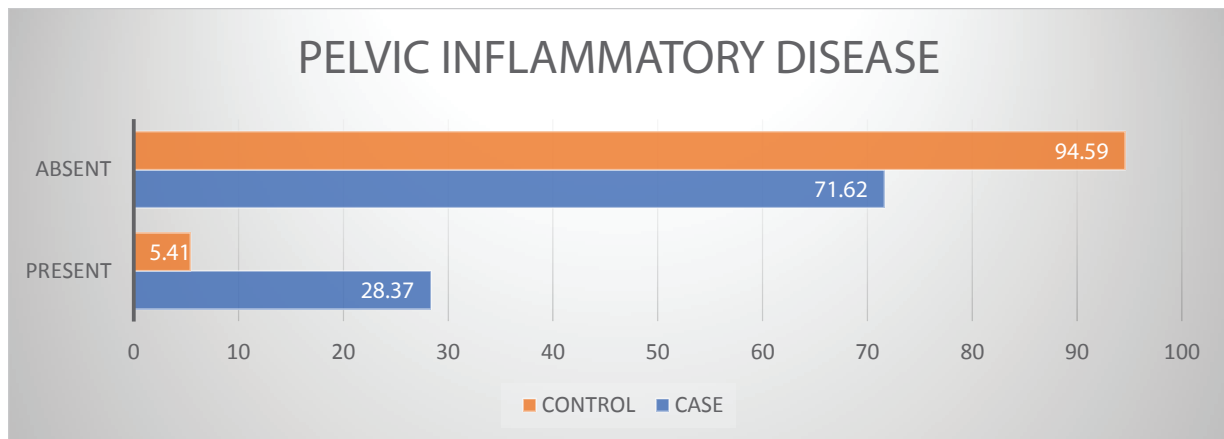


Figure 4 : Pelvic inflammatory disease and ectopic pregnancy

Age is an important factor for predicting the chances of ectopic pregnancy. Anorlu R I et al⁸ and Kopani et al⁹ have reported the mean age of ectopic pregnancy as 27.8 ± 6.21 and 30.37 years respectively. The mean age in our study was in the age group of (25-29) years. Actually, this age group is sexually more active and therefore there are maximum pregnancies, both intra-uterine and ectopic, in this age group. In our study 78.4% of the cases were multi-gravida. This is almost same with the study conducted by Panchl D et al¹⁰ who found ectopic pregnancy in 81.66% of multi-gravida women. With increasing gravidity, there is

significant reduction in the tubal motility, higher chances of anatomical distortion, poor hormonal control, physical capability etc. may cause higher chances of ectopic pregnancy.

In present study 4.05% cases had multiple sexual partners. This finding is not in concurrence with the study conducted by Bouyer J et al¹¹ and Anorlu RI et al⁸. They found history of multiple sexual partners in 75% and 68% cases respectively. Differences in the regional, socio-economic, cultural factors, social stigma, and inhibition of admitting having multiple sexual partners may be the reason of such finding. Often

women with multiple sexual partners acquire STDs which affects the female genital tract and the process of reproduction significantly. This is directly related to cause ectopic pregnancy.

Considering the socio-economic strata from where our study population belong, we have found 62.16% of cases have some kind of addiction to tobacco - 20.27% of them have addiction of smoking bidi and cigarette, 13.5% chew gutkha. The study by Escobar-Padilla B *et al*¹² found that smoking before and during conception is one of the major risk factors of ectopic pregnancy with an OR of 18.33.

In our study 13.5% cases had history of infertility and undergone some kind of treatment, which is not comparable to the study conducted by Bouyer J *et al*¹¹ who found infertility in 30.13% cases. This may be because patients are not financially sound and, in many occasions, they do not report to the hospital. Use of ovulation inducing agents was present in 9.4% cases in present, which is higher than the study by Bu Z *et al*¹³, who noticed ectopic pregnancy with history of ovulation inducing agents in 2.62% cases compared to 0.99% of natural cycle.

Previous ectopic pregnancy was present in 9.45% cases in the our study which was similar to results shown by Hassan N *et al*¹⁴ (6.45%) and Abbas A *et al*¹⁵ (7.40%). In present study 87.5% who had a previous ectopic pregnancy, had come to hospital again with another ectopic pregnancy. A patient with a history with previous ectopic pregnancy has a grave chance to cause another ectopic pregnancy as Zhang D *et al* found in their study that compared to non-pregnant patients, patients who had salpingotomy for previous ectopic pregnancy was at higher risk for recurrent ectopic pregnancy.¹⁶ The underlying reason of the previous ectopic pregnancy also influences and involves the other tube unless the causative factor is corrected.

The studies conducted by Majhi AK *et al*¹⁷ and Aziz S *et al*¹⁸ observed prior abortion in 26.1% and 37.8% cases respectively, which was in concurrence to the present study (29.72%) cases. Previous induced abortion may have some role to cause ectopic pregnancy by changing the environment of the cervix & endometrial cavity and allowing infections by various organisms. Thus, it can be said that number of previous abortions has a proportional relationship with ectopic pregnancy. In our study we found 75% chance of having ectopic pregnancy with previous 2 induced abortion whereas it's 100% when it is ≥ 3 .

History of PID was associated with 28.37% cases in present study. This is in concurrence with the study conducted by Hassan N *et al*¹⁴ who found PID in 35.4% cases. PID could be found in many cases which were diagnosed from history, clinical examination, USGs and culturing high vaginal swab. Unhealthy lifestyle, lack of awareness, multiple sexual partners, pond and river bathing etc are major reasons for such high incidence of PID. A patient with PID has abnormal ciliary motility of the tubes and changed bio-chemical atmosphere due to extensive inflammation of the pelvis and the uro-genital tract.

Previous history of laparotomy for both gynaecological and non-gynaecological indications were found to be 10.8% and 6.75% respectively, which is comparable with the studies by Anorlu RI *et al*⁸ (23%) and Hassan N *et al*¹⁴ (26%). Previous surgeries may cause distortion of normal anatomy, adhesion etc which in turn are the causative factors for ectopic pregnancies. Previous caesarean section was present in 24.32% cases. This finding is quite comparable with the report of Lee KR *et al* also (13.4%).¹⁹ This relation may be due to adhesion in the peritoneal cavity, distortion of normal anatomy, caesarean scar pregnancy etc. Multi-centric study (case-control) in Shanghai reported

that use of contraceptives reduced the risk of both intra uterine and ectopic pregnancy. Although a meta-analysis by Mol F et al²⁰ showed that the risk of ectopic pregnancy may actually rise by the use of OCPs, IUCDs and female sterilisation, Bouyer J et al¹¹ reported a decreased risk of ectopic pregnancy with the use of OCP and LNG-IUS. In our study 56.75% used some mode of contraception in their lives - 41.89% used barrier method, 2.7% used IUCD and 6.7% used OCP. Bilateral tubal ligation was failed in 5.4% cases; among them 50% ligation was done laparoscopically. Higher incidence of ligation failure was may be due to inadequate expertise, improper procedure, poor quality materials used for the procedures, higher patients load etc. This is quite comparable with the incidence reported by others.^{21,22}

Conclusion

Many factors may influence the incidence and prevalence of ectopic pregnancy. Out of those some may have a major impact on the increased rate of ectopic pregnancy in India than other countries. In this study we found some significant risk factors like addiction, multiple sexual partners, history of previous ectopic pregnancy, history of pelvic inflammatory diseases etc. Putting up major resistances against these factors, educating women and the society will surely help us to curb the deadly conditions. A highly suspicious mind, proper clinical knowledge and idea about the local risk factors will be helpful to successfully manage the grave health problem.

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Abbreviation

- ART – Assisted reproductive techniques
 ECP – Emergency contraceptive pill
 EP – Ectopic pregnancy
 ICU – Intensive care unit
 IUCD – Intrauterine contraceptive device
 LNG-IUS – Levonorgestrel intrauterine system
 MTP – Medical termination of pregnancy
 OBGYN – Obstetrics & Gynaecology
 OCP – Oral contraceptive pill
 PID – Pelvic inflammatory disease
 POP – Progesterone only pill
 STD – Sexually transmitted disease
 USG – Ultrasonography