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Original Research Article

Clinical course of ectopic pregnancy: a tertiary centre experience

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ABSTRACT

Background: Ectopic pregnancy (EP) is one of the causes of maternal mortality and morbidity in the first trimester. EP is still a major challenge and its incidence is on the rise due to changes in lifestyle and advances in medical practice. The early diagnosis and treatment of this condition over the past two decades has allowed a definitive medical management of unruptured ectopic pregnancies even before there were clinical symptoms in these high-risk women.

Methods: It was a retrospective study of 100 cases of EP conducted in the Department of Obstetrics and Gynecology, Bowring and Lady Curzon Hospital, attached to Bangalore medical college, Bengaluru for a period of 3 years. The aim of the study was to study the incidence, risk factors, clinical profile and management of EP cases.

Results: Incidence of EP was 1.3% of all deliveries and 5.6% of gynecological surgeries. Peak age group was between 25-30 years (37%). Most of them were multiparous (83%), 58% of the patients had identifiable risk factors. 95% had amenorrhea, followed by pain abdomen in 81%, bleeding PV in 43%. 17% presented with shock. 91% patients presented with ruptured ectopic, 9% were unruptured. Unruptured cases were treated medically using Methotrexate. Laparotomy was done for ruptured cases. Commonest site of Ectopic was ampulla (81%). Salpingectomy was done for most cases (86%). No maternal mortality observed.

Conclusions: All high-risk women should be screened at the earliest with serum β -hCG and TVS. The impact on future fertility can be improved by focusing on primary prevention and early diagnosis before rupture.

Keywords: Ectopic pregnancy, Risk factor, Rupture, Salpingectomy, Tubectomy

INTRODUCTION

Ectopic pregnancy (EP) is defined as the pregnancy in which fertilized ovum implants other than the endometrial lining of the uterus. Incidence of EP ranges between 0.25% to 2% of all pregnancies.¹ Ectopic pregnancy is gaining greater importance because of its increasing incidence and its impact on women's fertility.^{2,3} Ectopic pregnancy remains the leading cause of maternal deaths in early pregnancy about 1 per 2000 EPs and accounting for 15% of all maternal deaths.⁴ The early diagnosis and treatment of this condition over the

past two decades has allowed a definitive medical management of unruptured ectopic pregnancies even before there were clinical symptoms in these high risk women.^{5,6}

The risk factors for EP includes pelvic inflammatory disease, progestin contraceptive, previous tubal surgery, induced abortion, previous tubal pregnancy, assisted reproduction, ovulation induction, salpingitis isthmica nodosa, smoking, and diethyl stilbestrol exposure.^{7,8} Most of the tubal pregnancies become symptomatic within 12

weeks, but a small number of them progress beyond this gestation and are diagnosed late.⁹

PID is the commonest cause of ectopic pregnancy. It may be due to Sexually transmitted infections, mainly chlamydia and gonorrhoea and others being post-abortal, puerperal or also secondary to an extra genital pelvic infection or prior abdominopelvic surgery. According to ACOG (1998), prior PID due to Chlamydia Trachomatis is the most common risk factor.¹⁰ Salpingitis Isthmica Nodosa is a non-inflammatory pathologic condition of the tube. The tubal epithelium extends into the myosalpinx forming a true diverticulum. There will be abnormal myometrial electrical activity over the diverticula favouring ectopic implantation. The risk of tubal pregnancy after any sterilization procedure is 5% to 16%.¹¹ Intrauterine Contraceptive Device (IUCD) prevent intrauterine pregnancy effectively, tubal implantation to a lesser extent and chances of ovarian pregnancy are more. Cu-T 380A and Levenorgestrel device have got the lowest rate of ectopic and progestasart has got the highest rate.¹² Progestational agents inhibit tubal motility and favors ectopic pregnancy.¹³ Smoking causes ectopic by delayed ovulation, altered tubal and uterine motility and altered immunity. DES exposure causes the tubal abnormalities like shortened and convoluted tubes, constricted fimbria, and paratubal cysts favours ectopic implantation. The risk of ectopic pregnancy increases in women who conceive via Artificial reproductive technique. The first IVF pregnancy, before the first IVF live birth, was a tubal ectopic pregnancy.¹⁴ Higher volume of transfer media or deep catheter insertion may predispose to tubal transfer. Tubal reconstructive surgery increases the risk of ectopic.

The recent studies have focused on molecular level factors. Alterations in the molecular dialog between the blastocyst and the site of implantation may lead to ectopic pregnancy. Some possible factors are lectin, integrin, matrix-degrading cumulus and their inhibitors, prostaglandins, host of growth factors, cytokines and their receptors and modulator proteins.^{15,16} Proper management of EP needs early diagnosis, resuscitation, timely treatment, and follow up. Early diagnosis of EP is a difficult task but can be possible with the help of quantitative beta human chorionic gonadotropin (beta hCG) level, transvaginal ultrasonography, and laparoscopy.^{17,18}

The objectives of the present study were to know the demographic profile and the risk factors with respect to the ectopic pregnancy, to know the clinical presentation of the ectopic pregnancy and to know the outcome of the ectopic pregnancy.

METHODS

This was a retrospective study conducted in patients with ectopic pregnancy admitted at Bowring and Lady Curzon Hospital attached to Bangalore medical college and

research centre for a period of three years from April 2014 to March 2017 after obtaining ethical committee clearance from the hospital authorities. All The cases of ectopic pregnancy were identified from the records in the gynecology ward, operating room and emergency unit. Their case files were retrieved from the Medical Record department of the hospital. The information on the age, parity, sociodemographic characteristics, marital status, highest level of education and gestational age at presentation were extracted from the case files. Detailed history regarding the risk factors, clinical presentations, General, systemic, abdominal and vaginal examination was done. treatment modalities (whether surgical or medical), intra-operative findings and outcomes of ectopic pregnancy.

Inclusion criteria

- The women who were diagnosed as ectopic pregnancy cases, who were in the reproductive age group of 15-45 years.

Exclusion criteria

- All intrauterine pregnancies.

During the study period, all known cases of ectopic pregnancy were evaluated. In cases of acute EP classic triad of amenorrhea, abdominal pain and vaginal bleeding were present. Other symptoms and signs found were nausea, vomiting, syncopal attacks, pallor, and features of shock, with tense and tender lower abdomen. The diagnostic tools of ectopic pregnancies were urine pregnancy test, culdocentesis and transvaginal ultrasonography (TVS).

Laparotomy was done for ruptured ectopic pregnancy. In unruptured cases, when beta HCG <2000 mIU/ml, mass <3.5cm size, with no fetal cardiac activity and hemodynamically stable patients, single dose of 50mg/m² body surface area intramuscular methotrexate was given. Efficacy of therapy was monitored by estimation of beta HCG on days 4 and 7. If serum BHCG level does not decline by 15% from day 4 to day 7 additional dose were used until serum beta-HCG became undetectable in weekly surveillance. The anatomic position of EP and the treatment modality of ectopic were evaluated.

After collecting the data, the risk factors, anatomic portion of ectopic pregnancies and treatment modality which consisted of medical or surgical were compared with others studies.

Statistical analysis

Data were collected and analyzed using Microsoft Office Excel (version 2007)) and expressed as percentages in the text and tables. Statistical analyses were performed by

using statistical package for social sciences (version 16/0).

RESULTS

The incidence of ectopic pregnancy in our study was 7.7 per 1000 live births.

Table 1: Demography and obstetric history.

Age (in years)	No. of cases (100)	%
16-20	10	10
21-25	26	26
26-30	37	37
31-35	18	18
>35	09	09
Socioeconomic status		
Upper	10	10
Middle	23	23
Lower	67	67
Gravida		
Primigravida	17	17
Multigravida (G)	55	65
Grand multipara (G≥4)	28	28
Gestational age at presentation (in weeks)		
≤4	05	05
5-6	34	34
7-8	37	37
>8	24	24

Table 2: The risk factors associated with ectopic pregnancy.

No. of cases	Risk factors	No. of cases	%
1	Prior induced abortion /MTP	35	35
2	Previous abdominopelvic surgery		
	Appendectomy	05	05
	Caesarean section	27	27
	Tuboplasty	02	02
	Myomectomy	01	01
	Tubectomy	07	07
4	IUCD	03	03
5	Smoking	01	01
6	Age >35 years	09	09
7	Infertility treatment		
	Ovulation induction	07	07
	IUI	02	02
	IVF	01	01
8	Multiple sexual partners	02	02
9	Previous ectopic pregnancy	03	03
10	Gynecological causes		
	PID	23	23
	Fibroid	05	05
	endometriosis	01	01
11	Unidentified	42	42

Table 1 shows demographic profile of 100 EP patients. The mean age of the women was 28.1 years. Peak incidence was between 26-30 years (37%). Married women accounted for 98%. EP was noted more in multigravida (55%) followed by grand multipara (28%) and then primigravida (17%). The range of gestational age was 3-12 weeks.

Table 2 shows various risk factors, out of which history Prior induced abortion /MTP was the most common risk factor present in 35 cases. No risk factors were noted in 42 cases.

Table 3: Clinical presentation of 100 cases of ectopic pregnancy.

Symptoms	No. of cases	%
Amenorrhea	94	94
Abdominal pain	81	81
Bleeding per vaginum	43	43
Syncopal attacks	22	22
Nausea/vomiting	30	30
Classic triad	46	46
Signs		
Abdominal tenderness	76	76
Pallor	52	52
Hypotension	27	27
Shock	17	17
Forniceal tenderness	74	74
Forniceal mass	48	48
Cervical motion tenderness	67	67

Table 3 shows clinical profile of 100 EP patients, most cases presented with history of amenorrhea (94%), pain abdomen (81%) and vaginal bleeding (43%). Nausea and vomiting was seen in 30% and syncopal attack in 22 cases.

On examination pallor present in 52% of cases. Abdominal tenderness was seen in 76%, cervical motion tenderness in 67%, fornicial tenderness in 74% and fornicial mass in 48%. Urine pregnancy test was positive in all the 96% cases.

Table 4 shows in the present study group hemoglobin <7 grams in 19% of the patients and >7 grams in 81% of the patients. Ultrasound showed evidence of rupture in 85% of cases and unruptured in 15% of the cases. In the present study 85% were ruptured, 11% were unruptured and 4% were tubal abortion. Blood transfusion was required in 63% of the patients. One patient underwent hysterectomy due to ruptured cesarean scar pregnancy.

Table 5 shows the different types of surgical treatment done for 100 ectopic patients, among 89 ruptured cases about 45 of them underwent Unilateral salpingectomy, 35 underwent Unilateral Salpingectomy and ligation of tube on contralateral side in multiparous patients, 3 underwent Unilateral salpingo-oophorectomy for ovarian ectopic

gestation, one of them underwent excision of rudimentary horn, one had fimbriectomy, 2 cases had salpingotomy and milking of the tube was done in one case. Among 11 unruptured ectopic cases methotrexate treatment was given and followed in 9 patients and 2 underwent unilateral salpingectomy.

Table 4: Investigations and postop morbidity profile.

Investigations	No. of cases	%
Haemoglobin		
<7g/dl	19	19
7-9.9 g/dl	41	41
10-10.9 g/dl	26	26
≥11g/dl	14	14
Urine pregnancy test (UPT)		
Positive	96	96
Negative	04	04
Ultrasound		
Done	84	84
Not done	16	16
Morbidity and mortality		
Present		Absent
Anemia	63	63
Wound infection	05	05
ICU admission	17	17
Require general anaesthesia	45	45
Blood transfusion		
Required	63	63
Not required	37	37
Acute renal failure	00	00
Mortality	00	00

Table 5: Surgical treatment in cases of ectopic gestation.

Condition of tube	Treatment	No. of cases	%
Ruptured (89%)	Unilateral salpingectomy	45	45
	Unilateral salpingo-oophorectomy	03	03
	Unilateral Salpingectomy+ligation of tube on contralateral side	35	35
	Excision of rudimentary horn	01	01
	Salpingostomy	02	02
	Fimbriectomy	01	01
	Milking	01	01
	Hysterectomy (ruptured cesarean scar pregnancy)	01	01
	Unruptured (11%)	Methotrexate treatment	09
Unilateral Salpingectomy		02	02

Table 6 shows different sites of ectopic gestation, Ampullary part of the fallopian tube was the most common site (81%), followed by isthmus in 12% of cases, ovarian ectopic in 3%, corneal/interstitium in 2%, fimbria in 1%, ruptured cesarean scar pregnancy in one

case and rudimentary horn in one case. Left tubal pregnancy was commonly observed in 61% of cases than the right tubal pregnancy.

Table 6: Comparison of site of ectopic pregnancies.

Site	Rose et al	Chow et al	Present study
Ampulla	56.9%	79.6%	81%
Isthmus	39.78%	12.3%	12%
Fimbria	-	6.2%	01%
Corneal/interstitium	1.07%	1.9%	01%
Ovarian	1.07%	-	03%
Heterotopic	1.07%	-	-
Rudimentary horn	-	-	1%
Caesarean scar pregnancy	-	-	1%

Table 7: Comparison of condition of the tube.

	Savitha Devi	Wills and Mohambal	Present study
Ruptured	30.77%	66%	85%
Unruptured	69.23%	34%	11%
Tubal abortion	-	-	04%
	Left	Right	
Side of the tube affected	61%	35%	
Ovary	03%	-	
Rudimentary horn	-	01%	

Intraoperative findings among 100 ectopic cases is tabulated in table 7 shows ruptured tube in 85 cases, hemoperitoneum present in 75 cases and fluid in POD in 10 cases, 11 cases were unruptured and 4 had tubal abortions.

Table 8: Comparison of incidence in different studies.

Authors	Year	Incidence
Paran Joshi	1965	1:151
Vinaya Pendse	1976	1:266
D'Mello	1988	1:214
ICMR	1990	1:250
Annamma Thomas et al	1999	10.2:1000 live births
Rose Jpphy et al	2002	15.2:1000 live births
Present study	2014-2017	7.7:1000 live births

Morbidity included anemia, blood transfusion and wound infection.

By reducing and identifying the risk factors and catching the patients at the earliest it is possible to improve the prognosis so far as morbidity, mortality and fertility are concerned.

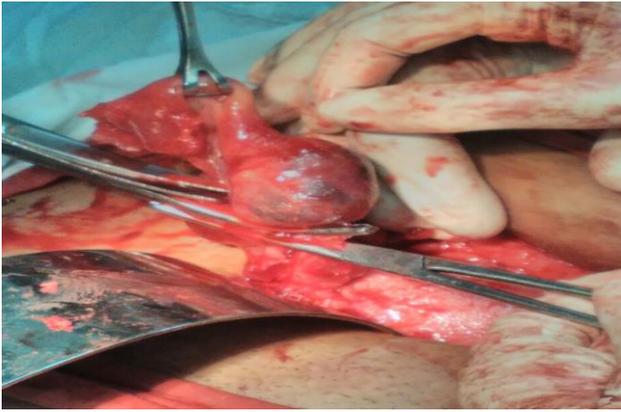


Figure 1: Right tubal ectopic gestation.

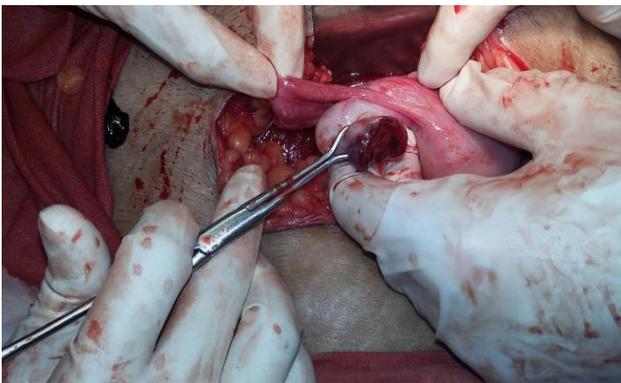


Figure 2: Left ovarian pregnancy.

DISCUSSION

Incidence of ectopic pregnancy is more in our hospital as it is a referral centre. It constituted 7.7 per 1000 live births as compared to 1.3% in Nigerian study by Udigwe et al and 0.6% in an Indian study by Arupkumar et al and 7.4% of gynaecological surgeries, which was comparable to 6.5% as in Nigerian study. The rate of EP was 1.9% as reported by Lozeau and Potter in USA, and 1.04% and 1% by Bangash and Ahmad and Waseem respectively, in Pakistan.¹⁹⁻²¹

In the present study, most of the patients belonged to the age group of 21 – 30 years, because in India most women marry at an early age, and hence fewer pregnancies are expected beyond the age of 30 years. Most of the patients were multipara in our study. Similar findings were noticed by Majhi AK and Roy N et al in their analysis of 180 cases of ectopic pregnancy.²²

Association of ectopic pregnancy with risk factors is observed 58% of the cases of the current study and the most common risk factor observed being previous abortion and prior D and C which reflected in 35% of the patients. In study done by Rose Jophy et al showed prior abortions and D and C contributed 25.8%.²³ Khaleeque et al also identified previous abortion (12.9%) as most

common risk factor in a similar study conducted by them.²⁴

About one third (42%) of patients in this study did not have any identifiable associated risk factor. It is evident that there may not be any tubal damage in many cases of ectopic pregnancy.²³ In these women the cause of ectopic pregnancy may be a dysfunction in the tubal smooth muscle activity.²⁵ Embryonic abnormalities have also been implicated in the attempt to explain the occurrence of ectopic pregnancy in the absence of tubal pathology. Classic triad of symptoms of EP was present in 43% of cases. History of amenorrhea was present in 94%. The most common symptoms at presentation were pain abdomen and bleeding per vaginam depicted in 81% and 43% of patients respectively. Similar findings were also observed in a study conducted by Chudary et al.²⁶

In present study, most of the ruptured ectopic gestations presented between 6 and 8 weeks. The abdominal pain which is due to peritoneal irritation is not unusual since most of the patients presented with ruptured ectopic pregnancy. The pain could be caused by tubal miscarriage and bleeding through the fimbrial end of tube into the peritoneal cavity. The pain could vary in intensity and usually does not necessarily reflect the volume of blood lost inside the abdominal cavity.²⁵ The absence of vaginal bleeding contributes to late presentation and the consequent rupture of the ectopic gestation.

Most common age group for ectopic pregnancy was 21-30 years (63%), as most of the reproduction and peak sexual activity occurs in this age which is similar to the study reported from Kaduna. The possible reason for this finding is that in recent years, the age at first conception has increased, which ultimately contribute to the increased incidence rate. Next common age group belonged to 30-40 years group (18%), which can be explained by ectopic pregnancies in post tubectomy cases and infertility cases. Majority of cases were multiparous (83%), highlighting previous Caesarean section (27%) and tubectomy failure (7%) as risk factors in present study. It seems that failure of tubectomy resulting in ectopic gestation is more common when it is done concurrently with caesarean section as documented in some studies. In a study conducted in France, tubal surgery and contraception were the main risk factors, while in another study by Ankum et al previous ectopic pregnancy and tubal surgery were found as risk factors.

Most common site of ectopic was ampulla (81%), which was comparable to Nigerian study (69.4%).²⁷ Now-a-days there is increase in incidence of ectopic gestation, especially ovarian pregnancy, heterotopic pregnancy and cesarean scar pregnancy. However, there is a decrease in mortality rate due to ectopic pregnancy due to improved facilities for diagnosis and management. But main Concern is subsequent infertility. Cesarean scar pregnancy was present in one case which presented with ruptured for which hysterectomy was done. In three

patients site of ectopic was ovary (3%), that was confirmed at laparotomy and by histopathological examination i.e. Spiegelberg criteria: 1. tube and its fimbriae normal and separate from pregnant sac 2. sac in the position of ovary 3. sac attached to uterus by ovarian ligament 4. histologically ovarian tissue recognised in wall of sac.

Majority of cases were ruptured (85%) at presentation as is usual in developing countries, which is more compared to the study done by Wills et al and Savitha Devi et al. In Latchaw G et al study, tubal rupture was present in 59% cases and 41% had unruptured ectopic pregnancies. Accurate diagnosis of unruptured ectopic pregnancy may help in the early treatment. They often present with pregnancy of unknown location, where β -HCG is positive, but ultrasound cannot confirm the location of pregnancy. Several bio-markers have been tried to confirm the diagnosis of early ectopic pregnancy.²⁸

The urinary pregnancy test, Serum β -hCG and ultrasound were the diagnostic tools used for diagnosis of ectopic pregnancy. Studies have shown that Ultrasonography should be the initial investigation for symptomatic women in their first trimester when the results are indeterminate, the serum beta HCG concentration should be measured. Serial measurement of β -hCG and progesterone concentrations may be useful when the diagnosis remains unclear.²⁹

Laparotomy was done in all ruptured cases. Salpingectomy remained the commonest surgical procedure for the management of ectopic pregnancy in our center which is similar to other centers in Nigeria.³⁰ Ipsilateral oophorectomy was only performed when the ovaries were diseased or involved in the adnexal mass. Conservative surgery is reserved for those with less tubal damage and contralateral tubal diseases, especially if they are nulliparous.³¹

Eleven (11%) patients presented early before rupture. 9 of them with mild symptoms were treated with methotrexate (MTX) 50mg im single dose, and were monitored clinically, by trans-vaginal sonography, and serum β -HCG levels on days 1 and 7. In various studies (Buster and Krotz- 2007) success rates with subsequent pregnancy for single and variable dose methotrexate were comparable to laparoscopic conservative surgery. MTX treatment of EP was safe and effective for selected patients with unruptured tubal EP, with no major side effects as found by Dhar et al.³² Salpingostomy was done in 2 cases to conserve the tube in Nulliparous patients, fimbriectomy in one, milking of the tube in 1 case and rudimentary horn excision in one case. Most common site of ectopic was ampulla (81%), which was comparable to Nigerian study (69.4%) and other studies.³³ Right sided tubal pregnancy was present in 35% cases and left tubal involvement in 61% cases, not same with other studies.³⁴ Morbidity included anemia, blood transfusion and wound infection. By reducing and identifying the risk factors and

'catching' the patients at the earliest it is possible to improve the prognosis so far as morbidity, mortality and fertility are concerned. No maternal mortality found in our study, consistent with A. Abbas and H. Akram study.³⁵ This is similar to the study carried out by Shetty and Shetty and Udigwe et al.^{36,37}

CONCLUSION

In conclusion, ectopic pregnancy has remained an important gynecological condition in our center. The most common identifiable risk factor was induced abortion in our study. Prevention should be aimed at health education, safer sexual practices and liberal use of contraceptives. Efforts should also be directed at prevention and adequate treatment of pelvic inflammatory diseases and sexually transmitted infections (STIs). The early diagnosis of an ectopic pregnancy is one of the greatest challenges for a physician. It requires a high index of suspicion to diagnose an ectopic pregnancy. The importance of an early diagnosis lies in the fact that the lady can be offered a conservative line of management which can definitely have a beneficial effect on her reproductive career

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