

# Spectrum of Ectopic Pregnancies at a Tertiary Care Center of Northern India: A Retrospective Cross-sectional Study

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## Abstract

**Objectives:** Diagnosis of ectopic pregnancy (EP) needs high index of clinical suspicion. If EP is timely diagnosed and timely intervened, i.e., before rupture, it may cause reduction of serious morbidity and mortality. We aimed to analyze the profile of patients of ectopic pregnancies and their outcome.

**Materials and Methods:** The sample for this retrospective cross-sectional study was derived from the database from January 2017 to December 2020. Data from outdoor patient registers, case record files, discharge summaries and hospital admission/discharge registers were screened. Parameters age, parity, risk factors, clinical presentation, per-operative findings, and maternal outcome in terms of morbidity and mortality were assessed.

**Results:** Totally 27,525 deliveries occurred during the study period of 3 years, of which 640 were ectopic pregnancies, i.e., 2.3%. Out of 640, 415 (64.8%) were acute ruptured ectopic pregnancies, 62 (9.6%) were chronic ruptured pregnancies, and 163 (25.4%) patients were unruptured ectopic pregnancies. The mean age was 28.67 years (range: 29.5–27.8). The most common site of rupture was ampullary (54%, 225/415). 14.8% (95/640) of cases were in hemorrhagic shock out of total ectopic patients, and in ruptured group, they comprised 22.8% (95/415). Success for medical management with single-dose methotrexate in our study was 90.2% (147/163).

**Conclusion:** Pelvic inflammatory disease and history of induced abortion were found to be the most important etiological factor in ectopic pregnancies. Comprehensive clinical examination is 100% sensitive in diagnosis of EP. In ultrasound, the presence of adnexal mass is the most common finding which is additive to clinical findings and not substitute. Although multiple management options are available, best outcome is attained if management of EP is done at earliest without any delay.

**Keywords:** Ectopic pregnancy, extrauterine pregnancy, methotrexate, tubal pregnancy

## INTRODUCTION

Ectopic pregnancy (EP) is a complication of first trimester of pregnancy in which embryo implants outside the uterine cavity. The incidence of EP in India is 0.91% of pregnant women (with no maternal deaths) in a study done at a tertiary care center in South India by Tahmina *et al.*<sup>[1]</sup> The most common risk factor is presence of pelvic inflammatory disease (PID) and history of abortions.<sup>[2,3]</sup> Diagnosis of EP needs high index of clinical suspicion because triad of amenorrhea, abdominal pain, and vaginal bleeding is

present only in 30%–40% of cases of ectopic pregnancies. If EP is not timely diagnosed and intervened, it may cause serious morbidity and mortality. Spectrum of EP ranges from asymptomatic cases to ruptured ones coming into shock. Delay in diagnosis can result in increased morbidity and sometimes even mortality. We present the data of ectopic pregnancies managed at our center over the last 3 years. This study was done with the aim of critically analyzing

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the etiology, clinical presentation, ultrasound findings, and management of ectopic pregnancies for better understanding of the disease and to find out lacunae in diagnosis and management if any.

## MATERIALS AND METHODS

This is a retrospective cross-sectional study derived from database at our department which is a tertiary care center. All the ectopic pregnancies (ruptured, unruptured, and chronic) managed at our center from January 2017 to December 2020 were included in the study. Ethical clearance was taken from the institutional review board (Reg. no.: ECR/262/Inst/UP/2013/RR-19) letter no. 1347/Ethics/2020 (Ref. code: 103 ECM II A/P8). For these outdoor patient data, case record files, discharge summaries, and hospital admission/discharge registers were screened. Waiver for consent form was granted from the ethical committee. Possibility of EP was suspected on clinical symptoms which were amenorrhoea, pain in abdomen or bleeding per vaginum. Positive signs were presence of adnexal mass and cervical motion tenderness, or hemoperitoneum on paracentesis. Ultrasound was done to assist the diagnosis, and common ultrasound findings considered for diagnosis were adnexal mass, gestational sac with or without cardiac activity in adnexa, free fluid in pelvic cavity, empty intrauterine cavity, pseudogestational sac sign, etc. The following parameters age, parity, risk factors, clinical presentation, per-operative findings, and outcome in terms of morbidity (hospital stay, blood transfusion, intensive care unit requirement, surgery, etc.) and mortality were assessed. For continuous variables, mean with standard deviation was used. For categorical variables, frequencies and percentages were used.

## RESULTS

Totally 27,525 deliveries occurred during the study period of 3 years, of which 640 were ectopic pregnancies, i.e., incidence of ectopic pregnancies at our center is 2.3%. Demographic characteristics in terms of age, parity, associated risk factors, and clinical presentation are illustrated in Table 1. The mean age of patients was 28.67 years (range: 29.5–27.8 years), and maximum patients were between the age group of 21 and 30 years. Maximum patients had parity of 1 (298, 46.4%). The mean gestational age (gestational age was calculated from last menstrual period) at presentation was 7 weeks. The maximum gestational age was found to be 12 weeks 5 days. The most common risk factors found were PID (30.2%) and history of abortions (27.3%). Out of 640 cases, 595 (93%) had a history of amenorrhoea while the rest of the 45 patients did not have any overdue menstrual history although bleeding history in present menstrual cycle was only spotting.

**Table 1: Demographic characteristics and clinical presentation of patients with ectopic pregnancies**

Characteristics	Ectopic pregnancies, n (%)
Age (years)	
18-20	115 (17.9)
21-30	298 (46.4)
31-40	128 (20)
>40	99 (15.4)
Parity	
0	89 (13.9)
1	398 (62.1)
2	111 (17.3)
3 or more than 3	142 (22.4)
Risk factors	
History of tubectomy	12 (1.8)
History of infertility treatment	8 (1.2)
History of previous ectopic	9 (1.4)
History of ATT intake	6 (0.9)
Previous laparotomy	9 (1.4)
History of induced abortion	179 (27.3)
Pelvic inflammatory disease	198 (30.2)
Clinical presentation	
Classic triad	249 (39)
Amenorrhoea	595 (93)
Abdominal pain	524 (82)
Vaginal bleeding	326 (51)

ATT: Antitubercular treatment

Five hundred and twenty-four (82%) patients had lower abdominal pain. Thirteen patients had typical vasovagal attacks. Four hundred and fifteen (64.8%) patients had a history of severe abdominal pain while 63 (9%) had heaviness in lower abdomen. Cervical motion tenderness was present in 49.4% of cases. Urine pregnancy test was done for all patients, and it was positive in 98% of cases. In rest 2%, laparotomy was done in the presence of hemoperitoneum and EP was confirmed histologically. Examination included both clinical and radiological (ultrasound) methods. Clinical examination was done in all patients, and clinical signs were diagnostic for 100% of cases. For all patients, ultrasound was also done and the most common presentation was presence of adnexal mass (93.12% of cases). Localization of embryo was possible in 28 cases (4.3%). Out of these 28 cases, 24 were diagnosed as tubal ectopic and 4 were diagnosed as ovarian EP. Four hundred and fifteen (64.8%) cases had free fluid in pouch of Douglas and 15% had free fluid till Morison's pouch. Out of 640, 415 (64.8%) were acute ruptured ectopic pregnancies, 62 (9.6%) were chronic ruptured pregnancies, and 163 (25.4%) patients were unruptured ectopic pregnancies. 14.8% (95/640) of cases were in hemodynamic shock out of total ectopic patients, and in ruptured group, they comprised 22.8% (95/415). 45.3% (188/415) of patients had severe anemia (hemoglobin <6 g %) while 31.8% (132/415) had moderate anemia (hemoglobin <8 g %). All ruptured

ectopic patients were taken for laparotomy in emergency. In laparotomy, amount of blood loss was in the tune of more than 2 L, found in 33.5% of patients. 32.5% of patients had blood loss between 1 and 2 L and 34% had blood loss <1 L. Per-operative findings according to site of ectopic pregnancies are mentioned in Figure 1. 93% (264/283) of ampullary and isthmic ectopic pregnancies were managed by salpingectomy while 6.9% (17/283) had salpingostomy. All 27 cornual pregnancies were managed by cornual wedge resection and none required hysterectomy. Out of six ovarian pregnancies, five were managed by ovarian wedge resection, while in one patient, oophorectomy was needed. Other rare types of ectopic pregnancies seen were as follows. Out of two cervical ectopic pregnancies, one cervical EP was managed medically and one had hysterectomy due to massive hemorrhage. There were three cesarean scar pregnancies, out of which two required hysterectomy and one was managed medically. All ruptured ectopic patients required blood transfusion which ranged from minimum one transfusion to maximum seven transfusions. Overall complications are mentioned in Table 2. There was no mortality. A total of 62 patients were of chronic EP, out of which 23 were managed laparoscopically and 39 patients were converted to laparotomy. Totally 163 patients were admitted with unruptured ectopic pregnancies and all were fit for medical management with intramuscular methotrexate according to the following criteria (serum beta-human chorionic gonadotrophin [HCG] <5000 mIU/ml, adnexal mass size <4 cm and absent cardiac activity, hemodynamically stable patient) [Figure 2]. One hundred and forty-seven patients (90.2%, 147/163) had successful outcome with

medical management while 16 (9.8%) patients required surgical intervention. Out of 16 patients, 14 had persistently rising serum beta-HCG and 2 had acute onset of abdominal pain and deterioration of vitals.

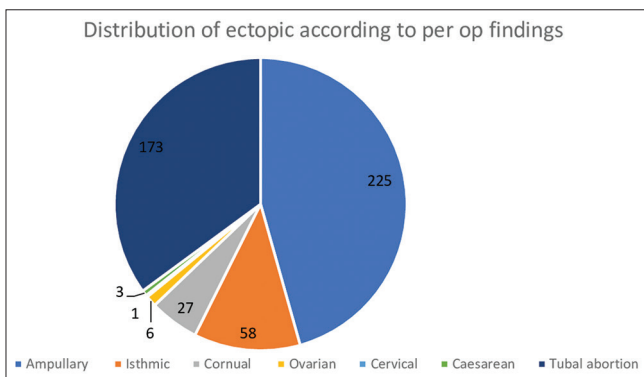
### DISCUSSION

The incidence of EP in our study was found to be 2.3%. Various studies have shown it in range of 1%–2%.<sup>[2,3]</sup> The reason for incidence toward higher side at our center is because of high number of referrals. In our study, 64.2% of patients had one or two associated risk factors, which is in concordance with other studies which have also shown it to be 66%.<sup>[4]</sup> However, Barnhart had shown in his study that 50% of patients had no risk factors.<sup>[5]</sup> Maximum patients (30.2%) had PID followed by history of induced abortion (27.3%) as a risk factor in our study. Explanation for high incidence of PID and induced abortions in our patients is because maximum patients are referred from low socioeconomic strata and they are multiparous women. Higher incidence (41.2%) of PID is also found in Seo *et al.* study.<sup>[6]</sup> However, PID as a risk factor for ectopic pregnancies is found in other studies only in the tune of 15%–20% although induced abortions are 36%.<sup>[1]</sup> The recurrence of EP in our study was 1.4%, and in literature, it ranges from 2% to 4%. Lesser incidence of recurrence of ectopic may be explained by strict vigilance regarding compliance for contraception after first EP treatment. Maximum patients who had recurrence did not follow contraception and two patients had tuberculosis.<sup>[1]</sup> The mean gestational age of EP in our study was 7 weeks. It was 7.3 weeks in a study by Seo *et al.*<sup>[6]</sup> while it was 6 weeks in a study by Khaleeque *et al.*<sup>[7]</sup> Amenorrhea is not present in 100% of cases of ectopic pregnancies. Seven percent of patients did not have amenorrhea in our study. In a study by Gharoro and Igbafe, 22.6% of patients did not have amenorrhea.<sup>[3]</sup> In a study by Smita Singh *et al.*, 52% of patients did not have amenorrhea. In the absence of amenorrhea, patients may be unaware of their pregnancy and medical professional needs high index of clinical suspicion in the presence of abdominal pain and irregular vaginal bleeding.<sup>[8]</sup> A classic triad of amenorrhea, abdominal pain, and vaginal bleeding was present

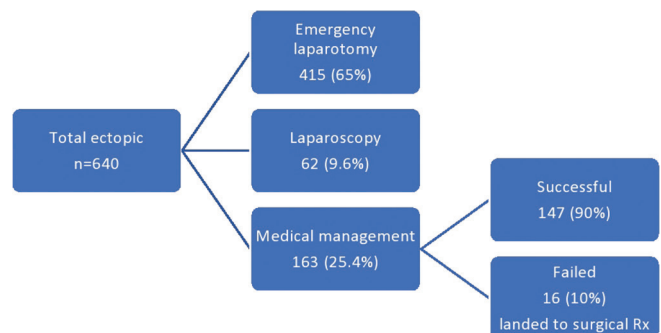
**Table 2: Complications in patients with ectopic pregnancies**

Morbidity	n (%)
ICU admission	101 (15.8)
Blood transfusion requirement	439 (68.5)
Wound infection	19 (2.9)
Transfusion-related lung injury (acute-onset noncardiogenic pulmonary edema)	3 (0.4)

ICU: Intensive care unit



**Figure 1: Distribution of ectopic according to type of ectopic pregnancy**



**Figure 2: Management according to type of ectopic pregnancies**

in 39% of cases only. Hence, diagnosis of EP requires strict clinical vigilance. In other studies, also triad was present only in 40% of cases. However, some studies have shown it in range of 28%–95%.<sup>[9]</sup> In our study, 64.8% (415/640) of patients required emergency surgical treatment in terms of laparotomy. Similarly, high rate of surgical treatment has been shown in other studies. Requirement of surgical treatment can be reduced if these pregnancies are early diagnosed and medically managed, as shown in a survey by Taheri *et al.*, Cornelius *et al.*, and van den Berg *et al.* studies.<sup>[10-12]</sup> The most common site of tubal ectopic was ampullary (52%), as also shown in other studies.<sup>[13]</sup> In our study, 64.8% of patients had ruptured ectopic and 93% had salpingectomy. Salpingostomy was done only in selected patients in whom either contralateral tube was absent or abnormal. Many studies have shown similar pregnancy rates after both salpingectomy and salpingostomy if contralateral tube is normal.<sup>[14,15]</sup> A randomized controlled trial by Mol *et al.* has shown statistically similar recurrent EP rates after salpingectomy (5%) and salpingostomy (8%).<sup>[16]</sup> In our study, 27 cases (5.1%) had cornual pregnancy and all had wedge resection. No patient had uncontrolled bleeding and did not require hysterectomy. No cornual ectopic pregnant patient could be managed medically because all were ruptured ectopic pregnancies. The success rate for surgical treatment was 100%, as shown in other studies.<sup>[16]</sup> Sixty-nine patients (10.7%, 69/640) required ventilatory support. The minimum duration of ventilatory support requirement was 1 day and maximum was for 7 days. 68.5% required blood transfusion in our study, however, a study by Udigwe and Mbachu showed blood requirement in 100% of cases. Out of these cases, 0.58% of cases also had transfusion-related lung injury because of massive transfusion.<sup>[17]</sup> Although 15% of referred patients came in hemorrhagic shock, we had no mortality, and all patients could be successfully managed, but it definitely increases logistic burden in terms of ventilatory support requirement and blood transfusion requirement. If these cases can be diagnosed early and can be managed medically or surgically by minimal invasive techniques, it will cause major health benefits. Laparoscopic surgery has been proved to be safer in terms of lesser blood loss, lesser postoperative adhesions, lesser hospital stay, and early convalescence by many studies. But again, laparoscopic management will be best in patients who are hemodynamically stable. Management of EP has been upgraded since 1883 and mortality is decreased from 60% to 1%. Earlier laparotomy was developed as life saving procedure. Afterwards advances were developed as laparoscopy and medical management for treatment of ectopic pregnancies. Laparoscopy is now recommended approach in surgical candidates. However, early catch hold of the disease is required as many of the cases diagnosed and referred are still hemodynamically unstable. The range of mortality in various

studies is from 0% to 1.3%.<sup>[11]</sup> Mortality usually occurs due to delayed referrals and blood unavailability. The National Institute for Health and Clinical Excellence has estimated that two-thirds of maternal deaths due to ectopic pregnancies in the UK may have been associated with inadequate care. Sixty-two (9.6%, 62/640) patients had chronic EP in our study, while in other studies, 20% incidence of chronic ectopic has been shown in total ectopic pregnancies.<sup>[18]</sup> Diagnostic criteria were amenorrhea followed by irregular vaginal bleeding, settled vitals, presence of adnexal mass on per vaginal examination, and confirmation of adnexal mass on ultrasound. Out of 62 patients, 23 were managed laparoscopically and 39 needed laparotomies. Because of chronic inflammatory changes and adhesions, distorting anatomy, surgery is difficult in chronic ectopic pregnancies. Chronic ectopic is formed due to repeated hemorrhages in the gestational sac leading to disintegration and formation of a pelvic mass. A chronic EP is often symptomatically milder and usually has a protracted course. Differential diagnosis of chronic ectopic includes PID, endometriosis, or fibroid. One hundred and sixty-three patients were given methotrexate in our study. Out of 163 patients, 147 patients (90.2%) were successfully managed with single-dose methotrexate while 9.8% needed surgical intervention. Success rate with methotrexate therapy is comparable with other studies, which has been shown in range of 78%–96%. A meta-analysis of more than 1300 ectopic pregnancies reported that a significantly higher proportion of patients were successfully treated with the multiple-dose regimen (92.7% vs. 88.1%) with single-dose methotrexate, respectively, although with more adverse effects.<sup>[18]</sup> Out of 16 patients who were taken for surgical intervention, 14 had persistently rising serum beta-HCG and two had acute onset of abdominal pain and deterioration of vitals. In our study, the patients who had failed medical management, had beta HCG more than > 4500 IU/L. Once starting medical management, patients should be counseled appropriately and should have willingness to follow-up for proper management for best results.

To our best of knowledge, this study is analysis of huge number (640) of ectopic cases and largest till date available in literature, but limitation is that this is a retrospective study. In spite of advanced diagnostic and therapeutic options, yet 15% of referred cases were in haemorrhagic shock. If strict clinical protocols are followed patients can be better managed.

Ectopic pregnancies are a major cause of abnormal vaginal bleeding in first trimester. If timely diagnosed and treated, morbidity and mortality can be deduced certainly. In comparison to medical management, surgical treatment has increased morbidity. Hence, early diagnosis, time management, and avoidance of delay in referral are key

points for best management of these patients. In view of the presence of PID and history of induced abortions as the most significant risk factors, EP can be definitely avoided by controlling these risk factors. Since clinical examination is 100% sensitive, so high index of clinical suspicion for EP will be helpful in early diagnosis and best management.

## CONCLUSION

Pelvic inflammatory disease and history of induced abortion were found to be most important etiological factors in ectopic pregnancies. Comprehensive clinical examination is 100% sensitive for diagnosis of ectopic pregnancy. Best outcome of ectopic pregnancy is achieved if management is done at earliest without delay.

## Acknowledgment

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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