

Unruptured tubal ectopic pregnancy: analysis and management

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ABSTRACT

Background: From its indirect reference by Abulcasis and till the nineteenth century the ectopic pregnancy was known as a universally fatal accident. Many patients with early resolving ectopic pregnancies escape surgical treatment. Preservation of future fertility became possible with the introduction of conservative surgical procedures and with the use of methotrexate. Aim and objectives of the study were: to analyse the age group, gravida, risk factors, clinical presentation, treatment given and outcome of the unruptured ectopic pregnancy.

Methods: We studied twenty-five women admitted to our tertiary care hospital, through emergency or outpatient department with tubal ectopic pregnancy from January 2017 through September 2021.

Results: 25 cases were studied during a 5 years study period between January 2017 and September 2021 in a tertiary care hospital, Mumbai. Maximum incidence of tubal gestation occurred between the age group of 36-40 years (36%). Greater incidence was noted in multigravida accounting for 68%. Risk factors seen were advanced maternal age (36%) previous history of induced abortion (24%), previous history of abdominal or pelvic surgery in 20%. The typical triad of amenorrhoea, pain abdomen and bleeding were observed in majority of cases. Significantly a greater number of cases had ampullary pregnancy (52%), followed by cornual (24%) and fimbrial (24%). Out of 25 cases of unruptured tubal ectopic pregnancies, 68% cases were treated by purely surgical intervention while 8% cases were managed medically by methotrexate however in 24% cases, the medical treatment failed and they ended up having surgical intervention.

Conclusions: In conclusion, this study showed that medical treatment of unruptured ectopic pregnancy with systemic methotrexate seems to be an option for some patients with unruptured tubal pregnancy.

Keywords: Conservative management, Unruptured tuba ectopic pregnancy, Systemic methotrexate

INTRODUCTION

The first known description of an ectopic pregnancy is Al-Zahrawi in the eleventh century. The word "ectopic" means "out of place."²

Risk factor

According to American College of Obstetricians and Gynecologists (ACOG), risk factors associated with ectopic pregnancies include: previous ectopic pregnancy, prior fallopian tube surgery, previous pelvic or abdominal surgery, certain sexually transmitted infection (STIs),

pelvic inflammatory diseases, endometriosis, and previous history of induced abortion.³

Other factors that may increase a woman's risk of ectopic pregnancy includes: cigarette smoking, age more than thirty-five years, history of infertility and use of assisted reproductive technology, such as *in vitro* fertilization (IVF).

The clinical manifestations of ectopic pregnancy complicate the diagnosis because of its broadspectrum that runs from asymptomatic until acute abdomen and hemodynamic shock. The classic clinical trial is: abdominal pain, amenorrhea and vaginal bleeding. The treatment of ectopic pregnancy includes medical or surgical methods. Both are effective, but the selection depends on clinical situation, localization of ectopic pregnancy and diagnostic tools.

Methotrexate is the drug used for conservative treatment. Methotrexate is a folate antagonist; the role is to halt the cycle process of DNA and RNA reproduction by folic acid. At different concentration level of methotrexate, different cellular phase is affected, but mostly in S phase of cell cycle.

There are two commonly used regimens for intramuscular methotrexate, one is a multiple-doseregimen of one mg/kg of methotrexate every other day, alternating with 0.1 mg/kg of leucovorin rescue, for up to four doses, or a single-dose regimen based on the body surface area (fifty mg per square meter) without leucovorin rescue. Studies have been done to compare the two regimens and the result was that the difference between the two regimens are not statistically significant. But it is also stated that the side effects from the multiple-dose is higher than single dose.

Side effects

Methotrexate is associated with a range of side effects. These include bone marrow suppression (myelosuppression), ulceration of the mucous membranes (mucositis), nausea, vomiting, diarrhoea, reversible alopecia, hepatotoxicity, Stevens-Johnson syndrome and toxic epidermal necrolysis.

We would like to determine the best treatment option depending of ectopic pregnancy situation. We analyzed the cases treated by conservative treatment and surgical interventions.

METHODS

We studied 25 women admitted to our tertiary care hospital, through emergency or outpatient department with tubal ectopic pregnancy from January 2017 through September 2021. Data were collected in a preconceived format. Data were collected, tabulated and analyzed.

The following parameters: age, gravida, gestational age, risk factors, clinical presentation, findings on ultrasoundogram and at surgery and management associated with ectopic pregnancy were noted.

Setting of study

The retrospective study was performed in the department of obstetrics and gynaecology, tertiary care hospital, Mumbai, India.

Study population

All patients 18 years and above diagnosed with unruptured tubal ectopic pregnancy were the study population.

Inclusion criteria

All patients 18 years and above diagnosed with unruptured tubal ectopic pregnancy in the 5 years study period were included.

Exclusion criteria

Patients less than 18 years of age and patients diagnosed with ruptured ectopic pregnancy were excluded from the study.

RESULTS

Age

The maximum age of women registered with unruptured tubal ectopic pregnancy is 39 years old and the minimal age is 21 years. The maximum number with unruptured tubal ectopic pregnancy in the present series occurred between the age group 36 to 40 years (36%).

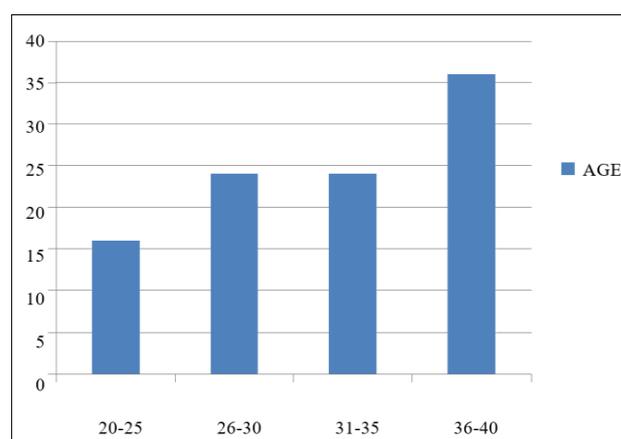


Figure 1: Ectopic pregnancy in relation to age.

Gravida

When review of previous reproductive performance was studied, it was found that the maximum incidence of

ectopic gestation (32%) occurred among the first gravida. In 8 out of 25 patients, ectopic pregnancy was the first conception.

Risk factors

Advanced maternal age was found to be the most common risk factor in my study accounting for nearly 36%. Previous history of induced abortion as the only risk factor was seen in 24% patient. Previous history of pelvic or abdominal surgery being the sole factor in 20% cases. Infertility as a risk factor was seen in 20% cases. 8% cases gave history of PID and they had undergone treatment with antibiotics and 4% patients had been operated previously for ectopic gestation or had undergone fallopian tube surgery in the past.

Table 1: Distribution of cases based on gravida.

S. no.	Gravida	No. of cases	%
1	Primigravida	8	32
2	Multigravida	17	68

Table 2: Risk factors in ectopic pregnancy.

S. no.	Risk factors	No. of cases	%
1	Previous ectopic pregnancy	01	04
2	Prior fallopian tube surgery	01	04
3	Previous pelvic or abdominal surgery	05	20
4	STIs	-	-
5	Pelvic inflammatory disease	02	08
6	Endometriosis	-	-
7	Cigarette smoking	-	-
8	Age older than 35 years	09	36
9	History of infertility	05	20
10	Use of ART (IVF)	01	04
11	Previous history of induced abortion	06	24

Table 3: Mode of presentation.

S. no.	Symptoms	No. of cases	%
1	Amenorrhoea	25	100
2	Pain in abdomen	16	64
3	Bleeding/spotting PV	16	64
4	Vomiting	02	32

Mode of presentation

The classical triad of amenorrhoea, pain abdomen and bleeding per vaginum was observed in majority of cases.

Amenorrhoea was the most significant symptom in all of patients. Vomiting was observed in 8% of the cases.

General physical examination table

12% cases presented with pallor. 28% were brought to the hospital in a state of shock (all shock indices exceeding >0.7) pointing towards a higher rate of morbidity in the form of ICU admission, requirement for blood transfusion and mortality in such patients.

Site of unruptured tubal ectopic pregnancy on laparotomy

Significantly a greater number of cases had ampullary ectopic pregnancy (52%) followed by cornual (24%) and fimbrial (24%) and none in the interstitial and isthmal part of fallopian tube.

Table 4: General physical examination.

S. no.	GPE	No. of cases	%
1	Pallor	3	12
2	Shock (shock index)	7	28

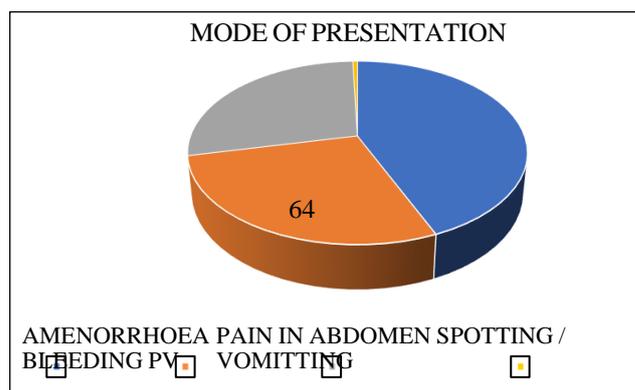


Figure 2: Mode of presentation.

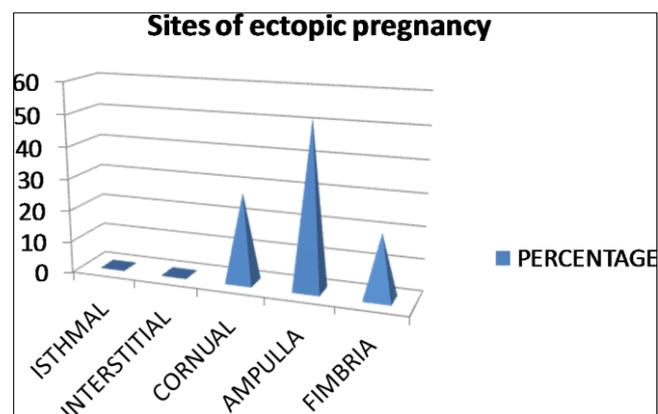


Figure 3: Sites of unruptured tubal ectopic pregnancy on laparotomy.

Blood group of patients with unruptured ectopic pregnancy

Majority of patients of unruptured ectopic pregnancy belonged to blood group O Rh positive (36%) followed by B Rh positive (32%) and A Rh positive (20%).

B Rh negative blood groups accounted for only 4% of cases.

Table 5: Blood group of patients with unruptured ectopic pregnancy.

S. no.	Blood group	No. of cases	%
1	A Rh positive	5	20
2	B Rh positive	8	32
3	AB Rh positive	2	08
4	O Rh positive	9	36
5	A Rh negative	0	00
6	B Rh negative	1	04
7	AB Rh negative	0	00
8	O Rh negative	0	0

Management of unruptured tubal ectopic pregnancy

Out of 25 cases of unruptured ectopic pregnancies 8 cases (32%) received conservative treatment with injection methotrexate, however during the course of conservative treatment only 2 cases (8%) were successfully treated whereas 6 cases (24%) failed due to inadequate or no response to injection methotrexate and rupture while under conservative treatment.

Table 6: Management of unruptured tubal ectopic pregnancy.

S. no.	Treatment	No. of cases	%
1	Successful medical t/t	02	08
2	Purely surgical t/t	17	68
3	Medical t/t failure	06	24

Morbidities observed

Blood transfusion was the most common morbidity observed amongst cases of unruptured ectopic pregnancy in current study.

Table 7: Morbidities observed.

S. no	Morbidity	No. of cases	%
1	Blood transfusion	20	80
2	ICU admission	-	-
3	Wound infection	-	-
4	Methotrexate related toxicity	-	-

DISCUSSION

According to ICMR multicentric case control study (1990) of ectopic pregnancy, majority of women were young and had low parity, while in the present study, the greatest incidence of unruptured ectopic pregnancy is observed in multigravida accounting for 68%.¹⁰

Pal et al in their study showed that the incidence of unruptured ectopic pregnancy was maximum in the 26-30 years age group (37.6%).⁵ In a study conducted by Wakankar et al to study ectopic pregnancy it was observed that the mean age of patients diagnosed with ectopic pregnancy was 29 years.⁶ Jacob et al, Murugesan et al and Shetty et al showed that most of the patients in their study belonged to 21-30 years of age group.⁷⁻⁹ This was dissimilar to the current study finding in which the majority of patients are in age group of 36-40 years. Similar results were observed in few studies from the United States of America which reported an increased ectopic pregnancy incidence with advancing age.¹¹

In the present study, the most common risk factor was advanced maternal age (36%) followed by previous history of induced abortion in 24% cases and history of abdominal or pelvic surgery in 20% cases. According to ACOG (1998), prior PID especially that caused by chlamydia trachomatis was the most common risk factor of ectopic pregnancy.¹² The ectopic pregnancy consisted of a wide range of symptoms. In the present study classical triad of symptoms was seen in majority (64%) of patients, however Pranathi et al, Jabbar et al and Zuber et al in their studies had reported that this triad was present in 28-29% of the study population.¹⁴⁻¹⁶

In the present study, 68% of the cases were managed surgically, mainly salpingectomy and 32% of the patients received medical treatment, however during the course of conservative treatment only 2 out of 8 cases were successfully treated whereas 6 out of 8 cases failed due to inadequate or no response to injection methotrexate and rupture while under conservative treatment. Belquis et al, Udigwe et al and Igwegbe in their studies had shown a similar higher rate of surgical management for unruptured ectopic pregnancy.^{17,18}

Majority of patients of ectopic pregnancy belonged to blood group O Rh positive (36%) followed by B Rh positive (32%).

Blood transfusion was the most common morbidity observed (80 %) in current study. Patients who were brought in shock (28%) and those who had anaemia (48%) (haemoglobin <10 gm%) were managed with both blood transfusion as well as plasma expanders. No patient showed any adverse drug reaction with injection methotrexate. Post-operative period was uneventful in cases which were surgically managed. Udigwe et al and Igwegbe et al in their studies had reported maternal mortality between 0-1.3% due to ectopic pregnancy,

however there was no maternal mortalities in the current study.¹⁷⁻¹⁹

The limitations of the study were that due to low sample size in the current study a more extensive study with large sample size was required to evaluate the condition and as most of the patients visiting our tertiary care hospital belonged to low socio-economic strata the results of this study cannot be generalized to the whole population.

CONCLUSION

Ectopic pregnancy occurs in around 1-5% of all pregnancies, and is associated with significant morbidity and mortality. The mainstay of diagnosis is by transvaginal ultrasound supported by serial serum human chorionic gonadotrophin (hCG) measurements. With growing experience, the management of unruptured ectopic pregnancy has moved away from surgery towards a more conservative (methotrexate) and expectant management in selected women that fulfil the criteria of medical management for unruptured ectopic pregnancy. An increasing number of patients with unruptured ectopic pregnancies are now seeking methotrexate treatment however, it is unclear which patients will benefit the most from it. Surgery, however, will always have a role in the management of women with unruptured ectopic pregnancy who are acutely unwell or where medical management is unlikely to be, or has been unsuccessful. As the incidence of ectopic pregnancy increases, ways and means have to be found to reduce the associated morbidity and mortality and to preserve future fertility. With emphasis shifting from radical to conservative therapy, prevention and early diagnosis become very important. Although ectopic pregnancy can never be eliminated completely, early diagnosis and prompt surgical or medical management will not only help in reducing maternal mortality and morbidity rates but also go a long way in preserving future fertility.

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