

FACTORS AFFECTING RUPTURED TUBAL PREGNANCY: A SYSTEMATIC REVIEW

Obstetrics & Gynaecology

Dr Nikhat
Khanam*

MBBS, Dr. Sulaiman Al Habib Hospital, Dubai, UAE *Corresponding Author

ABSTRACT

Ruptured Tubal Pregnancy is a life threatening gynaecological emergency that may be one of the cause of maternal mortality in the first trimester of naturally conceived pregnancy. Tubal Pregnancy is a type of Ectopic Pregnancy in which the fertilized egg implants itself in one of the fallopian tubes leading to an endanger of life due to tubal rupture as the egg grows. Several studies have identified various factors that lead to the occurrence of tubal rupture in an ectopic pregnancy. In this article various factors like previous ectopic pregnancy, infertility treatment, sociodemographic factors and various other maternal factors that have an association with tubal rupture have been identified and correlation has been established as to which risk factors are associated with ruptured tubal pregnancy.

KEYWORDS

Rupture, Tubal, Ectopic Pregnancy, Risk Factors

INTRODUCTION

Ruptured Tubal Pregnancy is a menacing condition which has lead to maternal mortality in the first trimester of naturally conceived pregnancy. The rupture of the tube mainly occurs in ectopic pregnancy in which the embryo has implanted in the fallopian tube and starts to grow in it. Once the fallopian tube is unable to accommodate it, it cause tubal rupture which may be a dangerous and serious condition for the mother.

Over the years many studies have been conducted to understand why ruptured tubal pregnancy occurs and through these various studies some identifiable maternal risk factors have been found which may have a correlation with the Ruptured Tubal Pregnancy. The various risk factors that have been seen to have an association with the rupture of tubal pregnancy are previous ectopic pregnancy, infertility treatment, sociodemographic maternal factors, beta-human chorionic gonadotropin(b-HCG) levels, tubal problems and a few others.

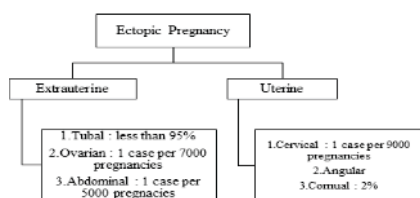
In this article we have discussed these various risk factors that have been associated with ruptured tubal pregnancy. The most commonly associated risk factors being fallopian tube injuries, infertility, contraceptive failure, smoking, age >35 years, previous ectopic pregnancy, and previous abortions.^[1]

Ectopic Pregnancy

Ectopic pregnancy, defined as the implantation of the embryo outside the uterine cavity, is a common, life-threatening gynaecological emergency. Worldwide, approximately 1–2% of all naturally conceived pregnancies result in ectopic implantation.^[2,3] Ectopic Pregnancy remains the leading cause of maternal mortality in the first trimester and accounts for 10–15% of all maternal deaths.^[4] It is very crucial to understand in case of ectopic pregnancy that it does not develop into a healthy pregnancy or a child rather it poses severe risk to the mother and thus an immediate medical line of action must be prepared to avoid risk and complications associated with ectopic pregnancy such as haemorrhage, rupture and infection which can be life threatening as well. It has been seen that > 30% patients with ectopic pregnancy suffer from infertility and 5-20% develop recurrent ectopic.^[5]

A. Epidemiology & Demographics^[6]

1. Incidence: 19 cases per 1000 pregnancies
2. Fatality rate: 4 cases per 10,000 ectopic pregnancies
3. Ruptured ectopic is leading cause of maternal death, accounts for 10% to 15% of maternal deaths.

B. Sites of ectopic pregnancies^[6]C. Clinical Presentation^[6]

1. Often symptomatic
2. Lower abdominal pain
3. Absent or irregular bleeding
4. Vaginal bleeding in 80% of patients
5. Presentation usually between 6 to 10 weeks after last menstrual period (LMP)
6. Shoulder pain
7. Dizziness, syncope, shock
8. Urge to defecate
9. Breast tenderness
10. Nausea

D. Management
Diagnosis

Even though the signs and symptoms of ectopic pregnancy has been well defined still a good correlation of these signs, symptoms and historical data is not enough to diagnose ectopic pregnancy. To confuse the diagnosis further, a normal menstrual history is reported in approximately 50% of patients with an ectopic pregnancy. A urine pregnancy test may occasionally be negative. Though rarely seen, the combination of a uterine decidual cast and a positive pregnancy test is virtually pathognomonic of an ectopic pregnancy.^[7]

Treatment

Treatment options for ectopic pregnancy include medical, laparoscopic, and laparotomy.

Methotrexate (MTX) therapy for ectopic pregnancy is a widely used medical alternative to surgery. Methotrexate is a folic acid antagonist that impairs DNA synthesis and cellular replication targeting rapidly proliferating cells such as trophoblasts.

There are three methotrexate treatment regimens that can be used : single-dose, two-dose, and multidose regimens. The side effects of MTX therapy occur in up to 30% of women but most of these resolve rapidly.^[8]

MTX is relatively contraindicated in patients with initial β -hCG levels of >5000 mIU/mL, a gestational sac size of >4 cm, presence of fetal cardiac activity and hemoperitoneum, which indicate a high treatment failure rate.^[9]

E. Potential Complications

The complications associated with ectopic pregnancy mainly is rupture of the tubule which leads to excessive bleeding in turn increases the chances of hypovolemic shock. It has been seen that in the first trimester of pregnancy the most common cause of pregnancy related deaths and 10% of maternal deaths is due to ectopic pregnancy.^[10]

Ruptured Tubal Pregnancy

I. Introduction

The most common extrauterine site of implantation of embryo is the fallopian tube in 95% of the cases of ectopic pregnancy. When the

embryo attaches itself to the fallopian tube it starts to grow inside the tube and as it grows the mass of the embryo starts to increase thus creating pressure on the fallopian tube. Eventually when the tubal lumen cannot accommodate the embryo it causes rupture of the tube leading to excessive bleeding and creating a life threatening condition.^[10]

II. Signs and Symptoms

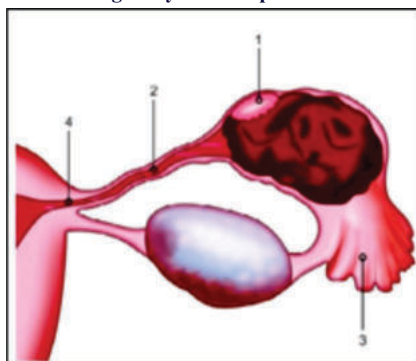
When an ectopic pregnancy causes a rupture, additional symptoms develop. Any of the following warrant an immediate visit to the emergency room:

- Sudden, severe abdominal or pelvic pain
- Dizziness or fainting
- Pain in the lower back
- Pain in the shoulders (due to leakage of blood into the abdomen affecting the diaphragm)^[11]



Figure 1: Signs and Symptoms of Ruptured Tubal Pregnancy^[11]

III. Sites of Tubal Pregnancy where rupture can occur:^[12]



- (1) The ampulla: 64%
- (2) The isthmus : 25%
- (3) The infundibulum : 9%
- (4) The intramural junctions : 2%

IV. Factors Affecting Ruptured Tubal Pregnancy

The knowledge of risk factors associated with the ruptured tubal pregnancy may be a valuable tool to identify women at risk for this life-threatening condition. As a result of surgical and medical advances such as laparoscopic management and methotrexate administration, we have seen a decrease in morbidity, lower costs, and fewer hospitalizations resulting from EP. Although it has long been recognized that EP accounts for significant morbidity and mortality. The widely used tools to establish the diagnosis of ruptured tubal pregnancy, such as tubal mass on ultrasound examination, heart rate, blood pressure, hCG and hemoglobin levels, are not always sufficient to predict it. Thus, Knowledge of the risk factors associated with the ruptured tubal pregnancy may be valuable to identify women who can be treated conservatively.^[3]

i. Previous Ectopic Pregnancy

Patients having history of ectopic pregnancy are more susceptible to tubal rupture if the 2nd pregnancy is also an ectopic pregnancy. It has been seen that patients with a history of ectopic pregnancy have damaged fallopian tubes which may pose greater risk and difficulty.

There are 2 main reasons that fallopian tubes in women that have had previous ectopic pregnancy might be abnormal.^[13]

- Ectopic Pregnancy usually happens when the fertilized embryo gets attached to the endometrium lining of the fallopian tube. So in some cases there is a possibility that the fallopian tube itself has an

anatomical defect such as scarring of tube which in turn does not allow the embryo to pass resulting in the embryo to get stuck in the tube before it reaches the uterus.

- The other scenario is when until the previous ectopic pregnancy the fallopian tubes were normal and the tubal pregnancy led to great damage of the inner lining of the tube.

Latcaw et al(2005) in his retrospective clinical trial on patients with ectopic pregnancy found out that patients with a history of a previous ectopic pregnancy are significantly more likely to experience a tubal rupture.^[13]

Roussos et al (2000) in his study also concluded that Rupture of the tube is more often observed in women with a history of ectopic pregnancy and in women with full-term pregnancy. Such observations suggest that ectopic pregnancy is less suspect in these cases.^[14]

Thus, it is important to consider Previous Ectopic Pregnancy as a risk factor of rupture in tubal pregnancy.

ii. Treatment of Infertility

Since fertility treatments are risk factors for ectopic pregnancy and since ectopic pregnancy is a risk factor for another ectopic pregnancy, treatment of ectopic pregnancy and how that treatment affects fertility is a complex issue.

In the treatment of infertility it has been seen that sometimes the surgical instruments are passed through the fallopian tubes which may result in the damage of the tube leading to rupture of the tube during a tubal pregnancy and it could also be a cause an ectopic pregnancy is developed.

iii. Tubal Problems or Diseases

Previous damage to the fallopian tubes is thought to be the cause of most ectopic pregnancies. Scarring in the tube prevents the normal passage of the fertilized egg through the tube and into the uterus where a healthy pregnancy takes place.

Pelvic Inflammatory Diseases infects the fallopian tubes, it can scar the lining of the tubes, making it more difficult for eggs to pass through. If a fertilised egg gets stuck and begins to grow inside the tube, it can cause the tube to rupture, which can sometimes lead to severe and life-threatening internal bleeding.^[15]

iv. Levels of Beta-HCG

In a normal intrauterine pregnancy, trophoblasts will secrete β -hCG with blood levels reaching 50–300 mIU/mL within two weeks of fertilization.^[16] The urine pregnancy test will generally become positive when the serum β -hCG is greater than or equal to 25 mIU/mL.^[16] In a normal early intrauterine pregnancy, the β -hCG level doubles approximately every 48–72 hours until about 60–90 days after conception.^[17] Only 15% of women with ectopic pregnancies will have serum β -hCG levels that rise in a way similar to normal intrauterine pregnancies.^[17] The most likely mechanism for low β -hCG levels in ectopic pregnancy is the degeneration of trophoblasts that result in cessation of β -hCG production.^[18]

Previous research has revealed that β -hCG levels >1750 mIU/mL was associated with a higher odds ratio (OR) for ruptured ectopic pregnancy.^[19] Another report showed that β -hCG levels >5000 mIU/mL was associated with an increased risk of ruptured ectopic pregnancy.^[13]

It was also seen in one of the studies that β -hCG levels failed to predict the risk of ruptured ectopic pregnancies.^[10]

A single very low serum level (< 100 IU/L) has been felt to be reassuring, in a review of 716 admitted patients with ectopic pregnancy, 29% of those with such a level were found to have tubal rupture at laparoscopy.^[20] The risk of tubal rupture was similar across a wide range of β -hCG values. Another study identified 38 instances of rupture among women with serum levels ranging from 10 to 189 720 IU/L.^[21] Thus, a single serum β -hCG measurement cannot exclude ectopic pregnancy or predict the risk of rupture unless it is less than 5 IU/L.^[22]

v. Obesity

In a recent study presented at the American Society for Reproductive

Medicine meeting, overweight women were 50% more likely to have an ectopic pregnancy (a pregnancy outside of the uterus, usually in the fallopian tube).

In a study by Fukami et al (2016) it was concluded that a Body Mass Index of more than 26 increase the risk of fallopian tube rupture.^[23]

vi. Haemoglobin Levels

When there is rupture of Ectopic Pregnancy there is blood loss which in turn results in the drop in the haemoglobin levels.

In a study by Knafel et al (2009), Low hemoglobin and hematocrit values, together with higher gravidity at the time of admission, may indicate an increased risk of tubal rupture.^[24]

vii. Location of Ectopic Pregnancy

Location of ectopic pregnancy may be associated with a higher incidence of ruptured ectopic pregnancies.

A previous study showed that ectopic pregnancies located at the cornua and isthmus were associated with a high incidence of ruptures.^[14] Interstitial pregnancy (IP) occupied 2% to 4% of ectopic pregnancies.^[25] Usually IP is considered a nonviable pregnancy, and has a 2.5% mortality rate due to uterine ruptured and severe bleeding.^[25]

However, in another study, the most common site of ectopic pregnancy was tube (bilaterally), which accounted for 78% and 90% in the unruptured and ruptured groups, respectively.

Therefore, tubal ectopic pregnancies had an increased risk of rupture.^[10]

viii. Gestational Age

In a study by Goksedef et al (2011), the mean gestation (in weeks) since the last menstrual period was significantly higher in patients with ruptured Ectopic Pregnancy compared with patients with unruptured Ectopic Pregnancy. Logistic regression analysis revealed that 6–8 weeks of amenorrhoea and >8 weeks of amenorrhoea was the significant risk factors for tubal rupture.^[3]

A retrospective study in Turkey found the odds of tubal rupture at gestational ages of 6–8 and greater than eight weeks to be 3.67 and 46.69, respectively.^[3] Other researchers observed a positive association of borderline significance between rupture and gestational age.^[26] This finding could be explained by the fact that the ectopic gestational mass generally increases with increasing gestational age, and rupture becomes more likely when the size of the gestational mass outgrows the fallopian tube.^[26]

V. DIAGNOSIS

Tests to identify an ectopic pregnancy, whether ruptured or not, may include:^[27-30]

- Pregnancy test
- Ultrasound
- Test of specific levels of pregnancy hormones in the bloodstream
- A sample of uterine tissue taken through a procedure known as dilation and curettage (D&C)
- Laparoscopic surgery to examine the inside of the abdomen

VI. TREATMENT

Unfortunately, ectopic pregnancies are not viable and require treatment to safely remove the embryo from the fallopian tube (or wherever else it has implanted outside of the uterus). Treatment options for ectopic pregnancy include medical management or surgery. Pharmacologic treatment with methotrexate can be used for early ectopic pregnancy when there is no risk of imminent rupture. Surgery is needed if the ectopic pregnancy has ruptured to repair any damage. With surgery, either only the pregnancy is removed from the tube or the entire tube is removed.

In ruptured ectopic pregnancy cases where a lot of blood has been lost, the patient may require a blood transfusion. Emergency treatment may require initial stabilization with oxygen, fluids, and elevating the legs above the level of the heart.

Over 95% of ectopic pregnancies occur in the fallopian tubes, and with the growth of the fetus, the pregnancy would invariably rupture

without medical intervention.^[31]

VII. Potential Complications

Possible complications or long-term effects of an ectopic pregnancy depend on many factors. The first concern is bleeding, and pregnant people are at risk of bleeding to death if emergency care is not sought in a timely matter.

Around 70% of people who have had ectopic pregnancies are able to become pregnant again (without assistance) even if a fallopian tube is lost through surgery. There is a risk of a recurrent ectopic pregnancy occurring between 10% and 20% of the time. The physician will probably recommend carefully monitoring during early pregnancy to determine where the embryo has implanted.^[32]

CONCLUSION

Ruptured Ectopic Pregnancy is serious life threatening condition with high maternal death rate and morbidity rate. Many patients do not have a proper documentation of their risk factors and no physical indication. It has been seen that most of the patients with ectopic pregnancy succumb to rupture of the tube leading to a condition which could endanger the life of the patient.

Thus a proper evaluation of its risk factors is important to determine the rupture at an early stage and preventing further loss.

List Of Abbreviations

	Abbreviation	Full Form
1.	Beta-HCG	beta-Human Chorionic Gonadotropin
2.	MTX	Methotrexate
3.	DNA	Deoxyribonucleic Acid

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