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**Review Article**

# Strategies to improve the early detection and management of ectopic pregnancies in primary care

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## ABSTRACT

Even in the advanced era of today, maternal morbidity and mortality are quite high; however, most pregnancy-related complications can be successfully prevented by early diagnosis and timely management. The primary care setting is of utmost importance in this regard, as it is the first line of contact between patients and physicians, and regular antenatal care services are provided by most of primary care settings. Ectopic pregnancy is one of the most prevalent pregnancy disorders and is further associated with high-risk complications and mortality. The clinical manifestations may mimic non-ectopic pregnancy conditions, making it difficult to develop diagnostic standards. However, ultrasonography and human chorionic gonadotropin (β-hCG) levels can ensure early diagnosis. Conservative treatment is pursued since surgical management is linked to multiple significant side effects. In most situations, pharmacotherapy using methotrexate in a single- or multi-dose regimen is the preferred course of treatment. Performing ultrasonography as soon as a pregnancy is confirmed to determine the location of the pregnancy, monitoring β-hCG levels, and ensuring prompt referral in the event of a possible ectopic pregnancy that cannot be treated conservatively are all important ways that primary care settings can play a significant role in early diagnosis and prompt management. Additionally, obstetric ultrasonography training for family physicians can help in the early detection of ectopic pregnancy, which can lead to favourable results. The purpose of this research is to review the available information about strategies to improve the diagnosis and management of ectopic pregnancy in primary care.

**Keywords:** Ectopic, Pregnancy, Primary care, Diagnosis

## INTRODUCTION

All medical disciplines have a strong interest in primary care today. Studies of issues presented to family physicians or general practitioners show that a significant share of the most prevalent issues are obstetric/gynaecological in nature.[1] Regular antenatal care services are provided by primary care settings to ensure a healthy pregnancy. Antenatal care offers a woman the first opportunity to interact with professional health services and further aids in referrals for women who experience complications. Each year, complications associated with pregnancy and childbirth result in 303,000 maternal fatalities worldwide. Antenatal care services significantly contribute to reducing maternal morbidity and mortality by diagnosing and managing pregnancy complications and additionally providing health education and promotion.[2]

Ectopic pregnancy is a prevalent pregnancy complication and is marked by improper implantation of the fertilized ovum in tissues other than the uterine endometrium. In almost 97% of instances, ectopic pregnancy is present in the fallopian tube, while it can additionally occur in the pelvic or abdominal cavities. Ectopic pregnancy rarely occurs in the cervix, while the ovaries and broad ligaments are less frequently mentioned. When a rupture occurs during the first trimester of pregnancy, this aberrant localization of pregnancy, which is a potentially fatal obstetrical disorder and affects women of reproductive age, becomes a major cause of maternal death. The incidence varies between 1 ectopic pregnancy per 28 live births and 1 ectopic pregnancy per 106 live births globally. The prevalence of ectopic pregnancies varies between studies and geographical locations.[3] The primary care physician is in an ideal position to identify and diagnose an ectopic pregnancy, as well as to guide patients on available treatments and possible risks. It is anticipated that the role of the primary care physician in treating patients with ectopic pregnancies will continue to expand given the trend towards outpatient nonsurgical management of ectopic pregnancies.[4]

Ectopic pregnancy is serious emergency that is frequently addressed by primary care physicians, although the diagnosis is frequently overlooked at the outset. Lower abdominal pain and vaginal bleeding in women of childbearing age frequently trigger the suspicion of an ectopic pregnancy, but occasionally individuals with vague symptoms who are unaware of an ongoing pregnancy may also exhibit hemodynamic shock. Patients with early pregnancy and risk factors should be referred to a tertiary care facility in the primary care setting to rule out ectopic pregnancy.[5] Expectant management, methotrexate medication, or surgery are all options for managing ectopic pregnancies. Methotrexate, however, is generally contraindicated in patients with initial β-hCG levels of >5000 mIU/ml, gestational sac size of >4 cm, existence of fetal cardiac activity, and hemoperitoneum, which point to significant failure rate for the therapy.[6]

Purpose of this research is to review available information about strategies to improve the diagnosis and management of ectopic pregnancy in primary care.

## METHODS

This study is based on a comprehensive literature search conducted on May 18, 2023, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about strategies to improve the diagnosis and management of ectopic pregnancy in primary care. There were no restrictions on date, language, participant age, or type of publication.

## DISCUSSION

Since ectopic pregnancy is the leading cause of pregnancy-related deaths in the first trimester, even a treating physician in a primary healthcare institution will benefit from having a basic understanding of its etiology and effective management.[7] A more thorough awareness of the rationale and the selection of patients for conservative management will help the patients, especially over the long term, with their future fertility.[8] This is because more patients with ectopic pregnancy are being diagnosed in the early stages owing to the increased use of high-resolution ultrasound and highly sensitive beta hCG assays. Individualized treatment should be provided for patients with unruptured ectopic pregnancy who are hemodynamically stable, while some of these patients can be safely treated in a primary care setting. The initial beta hCG value continues to be of utmost significance among all known markers of treatment outcome. Expectant management may be administered to women with initial values below 1500 mIU/ml, with a substantially higher likelihood of success for those with values below 1000 mIU/ml. A primary care physician can manage individuals with HCG levels under 1000 mIU/ml because rupture is less frequent in these patients. A single dose of methotrexate therapy is usually sufficient for women with values under 3000 mIU/ml when their values are below 5000 mIU/ml. On ultrasound, free fluid that is only present in the pelvis can still be handled non-surgically. Additionally, adnexal mass size should not be a barrier to providing non-surgical care.[9]

### *Evidence from literature*

Andolsek described that one of the most prevalent reasons why primary care physicians are accused of malpractice is that ectopic pregnancies are frequently misdiagnosed. Therefore, when risk factors like past ectopic pregnancies or pelvic inflammatory disease are mentioned, a more thorough evaluation of pelvic

problems should be conducted. If pregnancy is confirmed, it should be followed by an ultrasound examination to determine its location. Even when using a contraceptive, an ectopic pregnancy is still possible and is more likely to occur under these circumstances. All abortions need to be subjected to a pathologic examination, per the physician's orders. If there are no signs of pregnancy, an ectopic pregnancy should be excluded. When ectopic pregnancies are detected before rupture, timely referral is necessary to enable conservative tubal surgery.[10] While another study's authors defined that although ectopic pregnancy morbidity has decreased over the past 30 years despite an increase in incidence, it remains the leading cause of death in the first trimester of pregnancy. Therefore, early diagnosis is crucial, especially for women who are fertile and have risk factors for an extrauterine pregnancy. Amenorrhea, stomach pain, metrorrhagia, typical pregnant symptoms, and even syncope and shock are common symptomatologies. Clinical information, analytical data on mother's blood and urine, an ultrasound examination, transvaginal culdocentesis, laparoscopic or laparotomic inspection, and a histological analysis are used to make the diagnosis of ectopic pregnancy.[11]

Tahmina, Daniel, and Soloman stated that since the classic trio of amenorrhea, abdominal discomfort, and vaginal bleeding is rarely presented, a diagnosis requires a high index of suspicion. Women may present with unspecific symptoms, be unaware that they are pregnant, or even be in hemodynamic shock. Results from certain studies suggest that 3.5-7.1% of maternal deaths in developing nations are attributable to ectopic pregnancy.[12] A work-up should be done by a physician if a woman with a positive pregnancy test experiences abdominal pain and/or vaginal bleeding in order to securely rule out the potential of an ectopic pregnancy. Ultrasonography, particularly transvaginal ultrasound examination and measurement of the β-HCG, forms the basis of the diagnosis. Instead of the inability to visualize an intrauterine pregnancy, the ultrasound diagnosis is based on the visualization of an ectopic mass.[13]

High-resolution transvaginal scans (TVS) have made it possible to diagnose more clinically stable women with an ectopic pregnancy early, often before surgery is required. Therefore, early detection by TVS has the potential to save lives and can lower surgical morbidity by enabling elective surgery or even conservative non-surgical treatment alternatives. Instead of relying solely on the absence of an intra-uterine gestational sac, the diagnosis of ectopic pregnancy should be predicated on the positive detection of an adnexal mass by TVS. The vast majority of ectopic pregnancies will be identified at the initial scan if the early pregnancy pelvis is scanned systematically. In recent times, ultrasound, and in particular TVS, is becoming the new gold standard for diagnosing all types of ectopic pregnancy, and laparoscopy is no longer the gold standard for the diagnosis of ectopic pregnancy owing to TVS as a diagnostic tool. An expanded selection of conservative treatment options, such as pharmacological management and a wait-and-see expectant approach, are made possible by earlier diagnosis in clinically stable women. In fact, non-surgical therapy management methods have undergone a revolution as a result of the adoption of high-resolution transvaginal ultrasound technology.[14] Likewise, Mullany et al described that serum β-hCG levels are used as a diagnostic indicator for ectopic pregnancy in conjunction with TVS or transabdominal ultrasound results. In contrast to transabdominal scans, TVS has been demonstrated to be more sensitive and accurate in the diagnosis of early ectopic pregnancy. In particular, it was discovered that three-dimensional TVS paired with colour doppler ultrasound was superior to traditional 3D-ultrasound for the diagnosis of early caesarean scar ectopic pregnancy. Although imaging mimics make diagnosing ectopic pregnancy challenging, being aware of distinguishing characteristics on ultrasound enables more successful identification.[15]

Hendriks, Rosenburg, and Prine described the treatment of hemodynamically stable patients by family physicians in collaboration with their primary obstetrician as adequate. However, patients with an ectopic pregnancy that has ruptured and is exhibiting signs and symptoms of that should be shifted urgently for surgical procedures. Clinical findings, ultrasound results, and β-hCG levels should all be considered when deciding whether to manage the ectopic pregnancy medically or surgically. Treatment options for diagnosed ectopic pregnancy include pharmacological management with intramuscular methotrexate, salpingostomy, which is the elimination of the ectopic pregnancy while keeping the fallopian tube intact, or salpingectomy, which is the elimination of the affected or all fallopian tubes for the patient who are clinically stable, and the affected fallopian tube has not ruptured. Expectant management is uncommon but can be taken into consideration in patients with probable ectopic pregnancy who are asymptomatic and have very low and declining β-hCG values.[16]

Similarly, Sivalingam et al narrated that patients with an unruptured tubal ectopic pregnancy who are hemodynamically stable, have minimal symptoms, and have a decreased volume of free intraperitoneal fluid on an ultrasound scan can benefit from medical treatment. The most widely used and efficient medical treatment for ectopic pregnancy is intramuscular methotrexate, which is often given as a single dose. Methotrexate inhibits the growth of cytotrophoblast cells in ectopic pregnancy, lowering cell viability and β-hCG release and, hence, limiting progesterone support for the pregnancy. This makes tissue remodelling and ectopic pregnancy resolution easier. Patients need to be closely monitored to verify that the ectopic pregnancy has fully resolved. This requires serial measurement of β-hCG levels every 4-7 days until the level is less than 5 IU/l.72.[17]

Local prostaglandin, intravenous or local methotrexate, and local hyperosmolar glucose, as well as expectant

treatment, have been used successfully in some circumstances as conservative nonsurgical treatments for an early ectopic pregnancy. Success rate of conservative treatment has ranged from 71-100%, and after various forms of conservative treatment, 72-93% of patients achieved tubal patency. When emergency surgery is not required at time of admission and the serum hCG level is dropping, expectant treatment of early ectopic pregnancy is advised.[18] Masroor et al recommended that early-detected cervical pregnancy, which is a rare form of ectopic pregnancy, can be treated conservatively with intramuscular methotrexate and intrauterine potassium chloride injections without the need for curettage.[19]

Stabile et al. defined that most cases of early interstitial ectopic pregnancy can be managed conservatively and are related to basal serum levels. The pharmacological treatment involves the injection of methotrexate either systemically or locally, near or in the gestational sac, guided by ultrasound or laparoscopy, with a success rate that is dependent on the route of delivery and whether a single dosage or a multidose regimen is used. Since 1982, methotrexate has been well-known for its function in certain ectopic pregnancies. Even though the single-dose protocol has been described as a reliable course of treatment, few research studies have reported that the multidose regimen is more efficient. A pharmaceutical regimen utilizing methotrexate is generally effective, according to recent studies, however, there is insufficient evidence to support the use of a local or systemic strategy. With a reduced frequency of adverse effects, a smaller dosage, and a higher tissue concentration, local administration of methotrexate, whether transvaginal or laparoscopic, has the potential to be safer than systemic administration. However, it is more intrusive, necessitating specialized facilities and highly trained personnel.[20] While primary healthcare settings may not provide definitive management for ectopic pregnancies, a basic understanding of the pathophysiology and safe management enables healthcare providers to initiate appropriate steps, facilitate timely referral, and provide comprehensive care and support to women with suspected or confirmed ectopic pregnancies. Since the primary care setting is the first line of contact, they are in an ideal position to do so and make an early and timely diagnosis of ectopic pregnancy, thus preventing significant morbidity and mortality associated with it. However, the role of the primary care setting with respect to diagnosis and conservative management of ectopic pregnancy is poorly defined in the literature, as there is an increased scarcity of studies in this regard, which necessitates the immediate need for further research to highlight and signify the importance of the primary care setting in early diagnosis and prompt management of ectopic pregnancy.

## CONCLUSION

Ectopic pregnancy is a prevalent gynaecological condition that frequently affects otherwise healthy women and can have a high rate of morbidity and mortality. However, the morbidity and mortality associated with ectopic pregnancy can be successfully prevented with early diagnosis and prompt management. Primary care settings can play a vital role in this regard by critically evaluating the clinical manifestations of patients during routine antenatal visits, performing ultrasonography as soon as the pregnancy is confirmed to identify the location of the pregnancy, monitoring -hCG levels, and ensuring timely referral in cases of suspicion of ectopic pregnancy that cannot be managed conservatively. Furthermore, training family physicians in obstetric ultrasonography can also aid in the early and timely diagnosis of ectopic pregnancy, leading to favourable outcomes.

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