

Conservative Management of Ectopic Pregnancy: A Population Based Study in Saudi Arabia

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ABSTRACT

Background: Ectopic pregnancy occurs in 1-2% of all pregnancies and remains a significant cause of first-trimester pregnancy-related mortality, accounting for 10-15% of such deaths worldwide. Traditionally managed through surgical interventions, recent advancements in diagnostic technologies, including transvaginal ultrasonography and serial serum β -hCG measurements, have facilitated the development of conservative management strategies. These approaches, particularly medical management with methotrexate, offer a promising alternative to surgery by preserving fertility and providing effective treatment in carefully selected patients.

Patients and Methods: This prospective observational study was conducted at Gurrayat General Hospital over 2 years to evaluate the outcomes of conservative medical management for ectopic pregnancy using methotrexate. Patients received either a single-dose or multi-dose methotrexate regimen, and outcomes were assessed based on β -hCG levels, resolution time, and the need for surgical intervention.

Results: Out of 50 patients with ectopic pregnancy, 90% achieved successful resolution with methotrexate therapy. 64% received a single-dose regimen, with 81.25% achieving success, while 36% were treated with a multi-dose protocol, with 83.3% responding effectively. The mean time to resolution was 28 days, with the single-dose group showing a shorter resolution time compared to the multi-dose group. Minor side effects were reported in 6% of patients, and no severe methotrexate toxicity occurred. Five patients required surgical intervention due to treatment failure or clinical deterioration.

Conclusion: This study confirms that conservative management with methotrexate is a highly effective and safe treatment for ectopic pregnancy in appropriately selected patients, achieving a 90% success rate and minimizing the need for surgical intervention. Further research is needed to refine patient selection criteria and standardize treatment protocols.

Keywords:

Ectopic pregnancy, Methotrexate, Conservative management, Fertility preservation

INTRODUCTION

Ectopic pregnancy, a condition where a fertilized egg implants outside the uterine cavity, accounts for 1-2% of all pregnancies.¹ Despite its relatively low incidence, it remains a leading cause of pregnancy-related mortality in the first trimester, responsible for about 10-15% of such deaths globally.^{1,2} The most common site for ectopic implantation is the fallopian tube, although other sites like the cervix, ovary, and abdominal cavity are less frequently involved.³

Traditionally, ectopic pregnancy has been managed surgically, with salpingectomy or salpingostomy being the primary treatments. However, over the past few decades, advances in diagnostic techniques, particularly the use of transvaginal ultrasonography and serial serum β -hCG measurements, have enabled earlier detection of ectopic pregnancies. This has opened up opportunities for less invasive management strategies

in selected cases.⁴⁻⁶ Conservative management, including expectant management and medical therapy with methotrexate, has gained popularity for appropriately selected patients, especially those who are hemodynamically stable and have lower β -hCG levels.⁷ Studies suggest that medical management can be successful in 65-95% of cases, depending on the clinical criteria and early intervention. This approach not only reduces the need for surgery but also preserves the fallopian tube, which can be crucial for future fertility.^{7,8}

Despite these advances, there remains some controversy regarding the optimal criteria for selecting patients for conservative management, and outcomes vary based on geographic and institutional practices.^{6,8} This study aims to review the current strategies in the conservative management of ectopic pregnancy, assess success rates, and provide insights into future directions for improving patient outcomes.

PATIENTS AND METHODS

This was a prospective observational study conducted at Gurrayat General Hospital over a period of 2 years, from March 2016 to February 2018. The objective was to evaluate the outcomes and safety of

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conservative medical management using methotrexate in patients with ectopic pregnancies.

Inclusion criteria for medical management were based on the following:

- **Hemodynamic stability:** Only patients with no signs of internal bleeding or rupture were included.
- **Transvaginal Ultrasound Findings:** A confirmed diagnosis of ectopic pregnancy with an adnexal mass measuring less than 3-4 cm, without fetal cardiac activity.
- **Serum β -hCG levels:** Patients with initial β -hCG levels less than 5000 IU/L.
- **No contraindications to methotrexate:** Exclusion of patients with known hepatic, renal, or hematologic dysfunction.
- **Willingness for follow-up:** Patients agreed to regular outpatient follow-up, including serial β -hCG measurements and ultrasounds.

Exclusion criteria included:

- **Hemodynamic instability:** Presence of acute symptoms suggesting rupture or internal hemorrhage requiring surgical intervention.
- Ectopic mass greater than 4 cm, or detection of fetal cardiac activity.
- Pre-existing conditions contraindicating the use of methotrexate (e.g., significant liver or kidney disease, blood dyscrasias).

A total of 50 patients who met the inclusion criteria were included in the study. Patients were treated using a standardized methotrexate regimen. Two protocols were used based on initial β -hCG levels:

- **Single-dose Methotrexate Protocol:**

A single intramuscular dose of methotrexate (50 mg/m²) was administered on Day 1. β -hCG levels were measured on Day 4 and Day 7 post-administration. A successful outcome was defined as a 15% or greater drop in β -hCG levels between Day 4 and Day 7. If the β -hCG decline was insufficient (<15%), a second dose was administered, and monitoring continued.

- **Multi-dose Methotrexate Protocol:**

Used for patients with higher initial β -hCG levels (>3000 IU/L). Methotrexate (1 mg/kg) was administered on alternate days (Days 1, 3, 5, and 7), with leucovorin (0.1 mg/kg) given on the days between. β -hCG was monitored on treatment days, and success was defined as a significant reduction (>15%) after each dose. Patients were followed with weekly β -hCG measurements until β -hCG levels dropped to non-pregnant levels (<5 IU/L). Ultrasound was repeated as necessary to confirm the resolution of the ectopic mass. Outcome Measures:

The primary outcome of interest was the success of medical management, defined as the resolution of the ectopic pregnancy without surgical intervention.

Secondary outcomes included:

- Time to resolution (measured by days until β -hCG normalization).
- Number of methotrexate doses required.
- Complications, such as rupture or the need for emergency surgery.

RESULTS

A total of 50 patients diagnosed with ectopic pregnancy were included in the study. The mean age of the patients was 29.4 years (range 20-40 years). Of the 50 patients, 34 (68%) were multiparous, and 16 (32%) were nulliparous. The majority of patients (80%) had no significant medical history, while 10 (20%) had a prior history of ectopic pregnancy or pelvic inflammatory disease. 38 patients (76%) presented with lower abdominal pain, while 12 patients (24%) reported irregular vaginal bleeding. The average time from the onset of symptoms to presentation at the hospital was 6 days (range 2-10 days). The median initial serum β -hCG level was 2560 IU/L (range 500-5000 IU/L). 30 patients (60%) had β -hCG levels less than 3000 IU/L, while 20 patients (40%) had levels between 3000 and 5000 IU/L. Patients were treated according to either a single-dose or multi-dose methotrexate protocol: 32 patients (64%) were treated with a single-dose methotrexate regimen.

Table-1: Basic information of patients (n = 50)

Variable	Value
Mean Age (years)	29.4 (20-40)
Multiparous Patients	34 (68%)
Nulliparous Patients	16 (32%)
No Significant Medical History	40 (80%)
Prior History of Ectopic Pregnancy or PID	10 (20%)

Table-2: Clinical presentation of patients (n = 50)

Variable	Value
Presenting with Lower Abdominal Pain	38 (76%)
Presenting with Irregular Vaginal Bleeding	12 (24%)
Mean Time to Presentation (days)	6 (2-10)
Median Initial β -hCG Levels (IU/L)	2560 (500-5000)
Patients with β -hCG Levels < 3000 IU/L	30 (60%)
Patients with β -hCG Levels 3000-5000 IU/L	20 (40%)

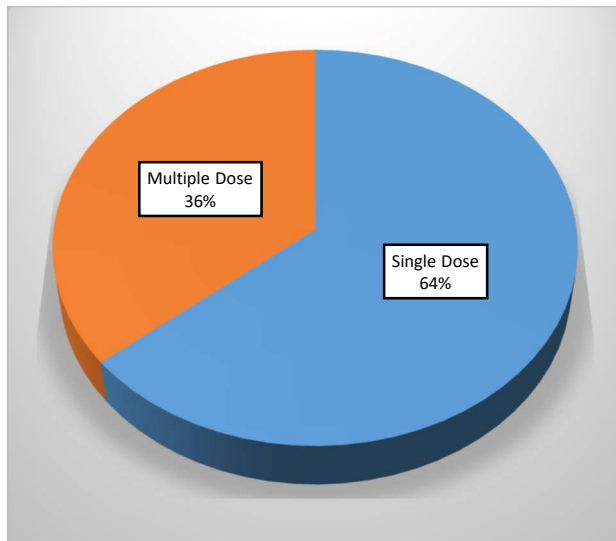


Figure-1: Dosing Regimen for Methotrexate

Of these, 26 patients (81.25%) showed a successful drop in β -hCG levels by Day 7. 6 patients (18.75%) required a second dose of methotrexate due to insufficient β -hCG decline. 18 patients (36%) with higher initial β -hCG levels (>3000 IU/L) were treated using the multi-dose protocol. 15 patients (83.3%) responded successfully, with adequate β -hCG declines after the second dose. 3 patients (16.7%) required additional doses or prolonged treatment but eventually had successful resolution without surgery. The overall success rate of medical management was 90% (45 out of 50 patients). 5 patients (10%) required surgical intervention due to methotrexate failure or clinical deterioration (e.g., signs of rupture or persistent β -hCG elevation). The mean time to resolution, defined as normalization of β -hCG (<5 IU/L), was 28 days (range 20-40 days). Patients in the single-dose group had a shorter resolution time (mean 25 days) compared to those in the multi-dose group (mean 32 days). 3 patients (6%) experienced minor side effects related to methotrexate, including nausea and mild abdominal discomfort, which resolved without intervention. There were no cases of severe methotrexate toxicity (e.g., hepatic or renal dysfunction).

DISCUSSION

Ectopic pregnancy remains a significant concern due to its potential for severe outcomes if not promptly and effectively managed. Traditionally, the standard treatment for ectopic pregnancies has been surgical, involving salpingectomy or salpingostomy. However, the advent of advanced diagnostic technologies such as transvaginal ultrasonography and serial serum β -hCG

Table-3: Outcome of patients undergoing conservative management of ectopic pregnancy (n = 50)

Variable	Value
Overall Success Rate	45/50 (90%)
Patients Requiring Surgery	5/50 (10%)
Mean Time to Resolution (days)	28 (Range: 20-40)
Mean Time to Resolution in Single-dose Group	25 days
Mean Time to Resolution in Multi-dose Group	32 days
Patients with Minor Side Effects	3/50 (6%)
Severe Methotrexate Toxicity	0/50 (0%)

measurements has enabled the shift toward less invasive approaches in appropriately selected patients.¹⁻³

This study provides valuable insights into the conservative management of ectopic pregnancy using methotrexate, highlighting its efficacy and safety in a population-based setting in Saudi Arabia. The findings align with global research that supports the use of conservative management strategies, particularly in hemodynamically stable patients with lower β -hCG levels and no fetal cardiac activity. The overall success rate of 90% reported in this study is consistent with the success rates observed in other studies, which typically range from 65% to 95%.⁹⁻¹² This high success rate underscores the effectiveness of conservative management for selected cases, particularly those with lower β -hCG levels and smaller ectopic masses. The choice between single-dose and multi-dose methotrexate protocols appears to be guided by initial β -hCG levels, with the single-dose regimen being effective for lower levels and the multi-dose regimen reserved for higher levels. This approach not only reduces the need for surgical intervention but also preserves fertility, which is crucial for many patients.

The safety profile of methotrexate in this study is reassuring, with only minor side effects such as nausea and abdominal discomfort reported. The absence of severe methotrexate toxicity further supports its use in conservative management. This is consistent with the broader literature that finds methotrexate to be a generally safe and well-tolerated option for managing ectopic pregnancies.^{11,13,14} The mean time to resolution

of 28 days observed in this study is comparable to the timeframes reported in other studies^{15,16}, though patients in the single-dose group experienced slightly faster resolution. The variation in resolution time between single-dose and multi-dose protocols reflects the different approaches to managing varying initial β -hCG levels and the associated therapeutic responses. This finding underscores the importance of tailoring treatment protocols to individual patient characteristics to optimize outcomes.^{14,16}

The study's inclusion and exclusion criteria are well-defined and align with current best practices for conservative management. However, the controversy surrounding the optimal criteria for patient selection remains a challenge. Further research and consensus on specific clinical criteria, such as exact β -hCG thresholds and ectopic mass size limits, could enhance the ability to identify patients most likely to benefit from conservative management. The study highlights that outcomes can vary based on geographic and institutional practices. This variability emphasizes the need for local guidelines and protocols that consider the specific resources and patient populations of different regions. The findings contribute to the ongoing discourse on standardizing conservative management practices while allowing for flexibility based on local contexts. Future research should focus on refining the criteria for selecting candidates for conservative management and exploring the long-term outcomes of patients who undergo medical management for ectopic pregnancies.

CONCLUSION

This study confirms that conservative management with methotrexate is a highly effective and safe treatment for ectopic pregnancy in appropriately selected patients, achieving a 90% success rate and minimizing the need for surgical intervention. Further research is needed to refine patient selection criteria and standardize treatment protocols.

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