



Alternative Follow-Up Regimen for Methotrexate Treatment is as Effective as Standard Follow-Up for Abnormal Pregnancies of Unknown Location



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INTRODUCTION

Adhering to day 4 and 7 post-methotrexate follow-up is a common challenge for patients, especially in under-resourced areas

OBJECTIVE

To compare outcomes of monitoring patients on days 4 and 7 to days 5 and 8 following methotrexate administration for confirmed ectopic pregnancies or pregnancies of unknown location.

Treatment success was defined as at least a 15% decline in serum human chorionic gonadotropin (hCG) between monitoring days, without surgical intervention.

METHODS

- Retrospective cohort analysis
- Years: 2016 and 2025
- Identified cases using ICD-10 diagnostic codes, followed by manual chart review
- Inclusion criteria
 - Confirmed ectopic pregnancy
 - Abnormal pregnancy of unknown location suspected to be ectopic
- Exclusion criteria
 - Initial hCG level greater than 5,000 mIU/mL
 - Planned two-dose methotrexate protocols
 - Lost to follow-up.
- Treatment success defined as a final hCG level less than 25 mIU/mL.
- Statistical analyses:
 - Fisher's exact test
 - Mann-Whitney U test

RESULTS

	Day 4/7 (n=100) n (%)	Day 5/8 (n=36) n (%)	Total (n=136) n (%)	p value
n	100	36	136	
Age (at time of methotrexate administration)	29.0 (5.5)	30.2 (5.1)	29.3 (5.4)	0.23
Patient race/ethnicity:				0.07
American Indian or Alaska Native	0 (0.0%)	1 (2.8%)	1 (0.7%)	
Asian	1 (1.0%)	0 (0.0%)	1 (0.7%)	
Black	27 (27.0%)	5 (13.9%)	32 (23.5%)	
Hispanic or Latino	0 (0.0%)	1 (2.8%)	1 (0.7%)	
Native Hawaiian or Pacific Islander	4 (4.0%)	0 (0.0%)	4 (2.9%)	
Other	16 (16.0%)	4 (11.1%)	20 (14.7%)	
Unknown	13 (13.0%)	10 (27.8%)	23 (16.9%)	
White	39 (39.0%)	15 (41.7%)	54 (39.7%)	
History of ectopic pregnancy:				0.78
No	86 (87.8%)	31 (86.1%)	117 (87.3%)	
Yes	12 (12.2%)	5 (13.9%)	17 (12.7%)	

	Day 4/7 (n=100)	Day 5/8 (n=36)
	Mean (SD)	Mean (SD)
Mean methotrexate dose (mg/m ²)	91.5 (13.3)	92.2 (13.7)
Mean initial hCG level (mIU/mL)	1350.2 (4327.9)	1341.1 (1512.7)
For those not requiring surgery, was methotrexate successful in treating the pregnancy?	n (%)	n (%)
With one dose	53 (53.0%)	21 (58.3%)
With two doses	37 (37.0%)	10 (27.8%)
How many patients whose hCG declined by 15% eventually required additional treatment	n (%)	n (%)
Surgical intervention required	8 (8.0%)	5 (13.9%)
Second dose of methotrexate required	40 (40.8%)	12 (33.3%)

- Of 319 patients identified, **136 met inclusion** criteria.
- There were no statistical differences in patient age at time of methotrexate administration, ethnicity/race, gravidity and parity, and history of ectopic pregnancy between the two cohorts.
- Baseline methotrexate dose and initial hCG were similar between groups.
- A $\geq 15\%$ decline in hCG occurred in 96.7% of the day 4/7 cohort and 91.3% of the day 5/8 cohort.
- In 41% of patients in the day 4/7 cohort and 33% of patients in the day 5/8 cohort, a second dose of methotrexate was needed.
- Surgery was necessary in 8% of patients in the day 4/7 cohort compared to 14% in the day 5/8 cohort.
- **Patients with a $\geq 15\%$ hCG decline had greater odds of treatment success (OR 3.95, 95% CI 1.21-15.3)**

Following up on days 5 and 8 or days 4 and 7 post-methotrexate treatment led to similar outcomes in ectopic or unknown location pregnancies.

DISCUSSION & CONCLUSIONS

- Patients had an **over 90% success rate** with methotrexate regardless of monitoring days, but a second dose of methotrexate was needed for over a third of patients.
- Limited by its small sample size and wide confidence intervals, though the similar raw outcomes between cohorts are reassuring. An additional limitation is our inability to assess why a patient followed up on days 5 and 8, rather than 4 and 7.
- Using a **threshold of 15% decrease between hCG levels appears more clinically significant** than monitoring on days 5 and 8 compared to days 4 and 7 following methotrexate administration.