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Original Research Article

PREDICTION OF OUTCOME OF SINGLE DOSE METHOTREXATE THERAPY BASED ON INITIAL AND DAY FOUR β-hCG LEVELS IN MEDICAL MANAGEMENT OF TUBAL ECTOPIC GESTATION

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ABSTRACT

Background: Ectopic pregnancy remains a major contributor to early pregnancy morbidity. Single-dose methotrexate is an established medical treatment, and early β-hCG dynamics may aid prediction of therapeutic response. The aim is to evaluate whether initial β-hCG level and day-4 β-hCG changes predict the outcome of single-dose methotrexate treatment in tubal ectopic gestation. **Materials and Methods:** A prospective observational study was conducted among 30 haemodynamically stable patients with tubal ectopic pregnancy managed with a single-dose methotrexate protocol in a tertiary care hospital over one year. Serum β-hCG levels were measured on days 1, 4, and 7. Treatment success was defined as resolution without additional methotrexate or surgery. Associations between β-hCG kinetics, sac size, and outcomes were analysed using chi-square tests and ANOVA, with $p<0.05$ considered significant. **Result:** Of 30 patients, 17 (56.7%) achieved resolution with a single dose, 3 (10%) required a second dose, and 10 (33.3%) underwent surgery. Responders had significantly lower mean β-hCG values at Day-1 (2075.6 ± 981.7 mIU/mL), Day-4 (1130.2 ± 723.5), and Day-7 (550.9 ± 593.5) than non-responders (Day-1: 3581.7 ± 503.4; Day-4: 3673.5 ± 634.9; Day-7: 4046.5 ± 674.0) ($p<0.001$). A decline in β-hCG from Day-1 to Day-4 occurred in 94.1% of responders versus 15.4% of non-responders. Smaller sac size (<2 cm) was also significantly associated with success ($p=0.004$). **Conclusion:** Lower initial β-hCG levels, smaller sac size, and early β-hCG decline are strong predictors of successful single-dose methotrexate therapy in tubal ectopic pregnancy. Early biochemical monitoring may support timely decisions regarding retreatment or surgery.

INTRODUCTION

Ectopic pregnancy occurs when a fertilised ovum implants outside the uterine cavity, commonly within the fallopian tube, and approximately 1–2% of all pregnancies.[1,2] It remains a major cause of first-trimester morbidity and mortality. Several risk factors including prior tubal surgery, previous ectopic pregnancy, pelvic inflammatory disease, use of certain contraceptive methods, assisted reproductive technologies, and smoking.[3] Clinical presentation differs from asymptomatic cases to acute, serious emergencies, highlighting maintaining a high suspicion, particularly among women with predisposing factors.[4] Improvements in serum β-human chorionic gonadotropin (β-hCG) assays and high-resolution ultrasonography have supported earlier and more accurate diagnosis, enabling timely intervention and improved reproductive outcomes.[3-5]

Methotrexate, a folate antagonist that inhibits DNA synthesis in trophoblastic tissue, has become the standard nonsurgical treatment for selected patients. Particularly advantageous for women who are haemodynamically stable and have an unruptured ectopic pregnancy. It offers high success rates, reduces treatment costs, minimises tubal damage, and preserves future fertility. The reported success rates for the single-dose regimen range from 64% to 94%.[6,7] Candidates typically meet criteria, including haemodynamically stable, serum β-hCG <5,000 mIU/mL, ectopic mass <4 cm, absence of foetal cardiac activity, and minimal or no pelvic free fluid.[8,9]

The single-dose methotrexate procedure involves administration of intramuscular methotrexate (50

mg/m²) on day 0, followed by β-hCG assessment on days 4 and 7. A decrease of ≥15% between days 4 and 7 indicates treatment success, whereas a second dose is recommended if this threshold is not met.[10] Continue β-hCG monitoring on days 11 and 14, then weekly until levels fall < 5 mIU/mL. This regimen is the most widely used for unruptured ectopic pregnancies, with success rates between 60% and 94%.[7,11-14]

Early β-hCG dynamics, particularly changes observed by day 4, may serve as stronger predictors of treatment success compared to baseline β-hCG alone. Elevated initial β-hCG levels have been strongly linked to treatment outcome as failure, with significantly lower success observed in patients with baseline levels ≥ 3,500 mIU/mL.[6] A Turkish study found a mean β-hCG level of 4,412 mIU/mL in failures versus 1,079 mIU/mL in successes ($p < 0.001$).[8] one study notes failure rates of 3.7% for <5,000 mIU/mL versus 14.3% for >5,000 mIU/mL with methotrexate,[7] Despite known links between baseline β-hCG and methotrexate success, studies vary in predictive accuracy using initial levels alone. Early day-4 β-hCG declines may be superior predictors, but evidence is limited. This study clarifies if values outperform baselines to optimize patient selection in single-dose methotrexate for tubal ectopic pregnancy. Therefore, this study aims to determine whether early β-hCG values, particularly the decline observed by day 4, predict successful outcomes more accurately than initial β-hCG values alone. Also, examines the influence of baseline β-hCG as an independent prognostic indicator in tubal ectopic pregnancies treated with single-dose methotrexate.

Aim

This study aimed to assess the efficacy of initial serum β-hCG level and the trend of day-4 β-hCG level in predicting the outcome of single-dose methotrexate therapy in the management of tubal ectopic gestation.

MATERIALS AND METHODS

This prospective observational study was conducted on 30 patients with tubal ectopic pregnancies at the Department of Obstetrics and Gynaecology, Government Rajaji Hospital and Madurai Medical College, Madurai, over a period of one year. The study was performed after obtaining clearance from the Institutional Ethics Committee. Informed consent was obtained from all patients before enrolling in the study.

Inclusion Criteria

Patients diagnosed with tubal ectopic gestation who were haemodynamically stable, had an initial serum β-hCG level of <5,000 mIU/mL, and a gestational sac measuring < 4 cm, no detectable embryonic cardiac activity and no free fluid in the cul-de-sac on ultrasonography were included.

Exclusion Criteria

Patients with haemodynamic instability, known hypersensitivity to methotrexate, immunodeficiency, active peptic ulcer disease, hepatic or renal dysfunction, or underlying pulmonary disease, breastfeeding women and those with an intrauterine gestation, initial β-hCG level > 5,000 mIU/mL, a gestational sac size > 4 cm, the presence of embryonic cardiac activity, or evidence of hemoperitoneum, and who refused to participate were excluded.

Methods: A detailed history was obtained from each patient, followed by a thorough clinical examination with emphasis on per abdominal and per vaginal assessment. Transvaginal ultrasonography was performed to determine the site of gestation, gestational sac size, presence or absence of embryonic cardiac activity, and any collection in the cul-de-sac. Venous blood (6 mL) was drawn from each subject under aseptic precautions, with samples collected into a purple EDTA vacutainer for complete blood count (analysed the same day) and a red plain vacutainer for renal and liver function tests as well as β-hCG estimation. Serum β-hCG levels were measured using the Access Immunoassay Systems by Beckman Coulter Access 2, using a chemiluminescent assay. The patients were assigned to two groups based on treatment outcome. Group A (Responders): Patients whose condition resolved with a single dose of Methotrexate (MTX). Group B (Non-responders): Patients who required a repeat dose of MTX or underwent surgical management due to a lack of adequate response to the initial dose.

Statistical analysis: Data were analysed using SPSS v25.0. Categorical variables were summarised as frequencies and percentages and compared using the Chi-square test or Fisher's exact test. Continuous variables were expressed as mean ± SD and analysed using One-Way ANOVA with post-hoc tests when required. β-hCG trends were categorised as increasing or decreasing and compared using the Chi-square. A p-value <0.05 was considered significant.

RESULTS

Age, gravidity, previous abortion, prior ectopic pregnancy, history of tubal surgery, PID, and contraceptive use showed no significant association with the success or failure of methotrexate therapy (all $p>0.05$). Gestational age showed a small association ($p = 0.055$), with earlier gestations (5–6 weeks) being more likely to resolve with a single dose, while later gestations (7–8 weeks). Sac size showed a significant association ($p = 0.004$), where smaller sacs (<2 cm) were associated with successful single-dose resolution, and larger sacs (>3 cm) were frequently linked to treatment failure and need for surgery [Table 1].

There was a significant difference in mean β-hCG levels between the three outcome groups at all

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measured time points (Day 1 to 7) ($p < 0.001$) [Table 2].

Table 1: Comparison of clinical and demographic factors with treatment outcomes

Variable	Category	Resolved with a single dose	Required second dose	Underwent surgery	P-value
Age (years)	<20	1 (3%)	0	1 (3%)	0.086
	21–25	7 (23%)	3 (10%)	2 (7%)	
	26–30	5 (17%)	0	7 (23%)	
	>30	4 (13%)	0	0	
Gravidity	G1	7 (23%)	2 (7%)	6 (20%)	0.453
	G2	6 (20%)	1 (3%)	3 (10%)	
	G3	4 (13%)	0	0	
	G4	0	0	1 (3%)	
H/O abortion	No	14 (47%)	2 (7%)	9 (30%)	0.628
	Yes	3 (10%)	1 (3%)	1 (3%)	
H/O ectopic pregnancy	Yes	1 (3%)	0	1 (3%)	0.815
	No	16 (53%)	3 (10%)	9 (30%)	
H/O tubal surgery	Yes	1 (3%)	1 (3%)	0	0.125
	No	16 (53%)	2 (7%)	10 (33%)	
H/O PID	Yes	1 (3%)	0	1 (3%)	0.815
	No	16 (53%)	3 (10%)	9 (30%)	
H/O Contraceptive use	Yes	1 (3%)	0	1 (3%)	0.815
	No	16 (53%)	3 (10%)	9 (30%)	
Gestational age (weeks)	5	6 (20%)	0	0	0.055
	6	7 (23%)	0	4 (13%)	
	7	4 (13%)	2 (7%)	5 (17%)	
	8	0	1 (3%)	1 (3%)	
Sac size (cm)	<1	1 (3%)	0	0	0.004
	1–2	8 (27%)	0	0	
	2–3	8 (27%)	1 (3%)	3 (10%)	
	>3	0	2 (7%)	7 (23%)	

Table 2: Mean β-hCG levels across treatment outcomes

Mean β-hCG levels	Resolved with single dose	Required to repeat the second dose	Underwent surgery	P-value
Day-1 β-hCG	2075.6 ± 981.7	3252.0 ± 330.4	3680.6 ± 516.2	<0.001
Day-4 β-hCG	1130.2 ± 723.5	3188.0 ± 225.9	3819.2 ± 651.1	<0.001
Day-7 β-hCG	550.9 ± 593.5	3301.3 ± 211.1	4336.1 ± 710.2	<0.001

Group A predominantly showed decreasing β-hCG levels over time, with 47% < 1000 IU/L by Day-7 (initial: 3/30 [10%]; Day-4: 10/30 [33%]; Day-7: 14/30 [47%]). In contrast, Group B showed higher β-hCG values, with all patients ≥3000 IU/L by Day-7 (3001–4000 IU/L: 7/30 [23%]; >4000 IU/L: 6/30 [20%]) [Table 3].

Table 3: Distribution of β-hCG levels across treatment outcome groups

Variable	Category	Group A	Group B
Initial β-hCG Level	<1000	3 (10%)	0
	1001–2000	4 (13%)	0
	2001–3000	7 (23%)	3 (10%)
	3001–4000	3 (10%)	8 (27%)
	>4000	0	2 (7%)
Day-4 β-hCG Level	<1000	10 (33%)	0
	1001–2000	4 (13%)	0
	2001–3000	3 (10%)	1 (3%)
	3001–4000	0	7 (23%)
	>4000	0	5 (17%)
Day-7 β-hCG Level	<1000	14 (47%)	0
	1001–2000	2 (7%)	0
	2001–3000	1 (3%)	0
	3001–4000	0	7 (23%)
	>4000	0	6 (20%)

An increasing level of β-hCG was seen between Day-1 and Day-4 in Group B, especially among those with initial levels 3001–4000 mIU/mL (23.3%) and >4000 mIU/mL (6.7%). In contrast, a decreasing between Day-1 and Day-4 was mainly observed in Group A, with the highest proportions in the 2001–3000 mIU/mL (20.0%) and 1001–2000 mIU/mL (13.3%) categories. Similarly, between Day-4 and Day-7, an increasing trend was again concentrated in Group B (notably 3001–4000: 16.7%; >4000: 6.7%), while Group A showed a decreasing trend across nearly all categories [Table 4].

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Table 4: Comparison of serial β-hCG levels (Day-1, Day-4, Day-7) between the groups

Variable	Category	Group A	Group B
Increasing trend of β-hCG between Day-1 & Day-4	<1000	0	0
	1001–2000	0	0
	2001–3000	1 (3%)	2 (7%)
	3001–4000	0	7 (23%)
	>4000	0	2 (7%)
Decreasing trend of β-hCG between Day-1 & Day-4	<1000	3 (10%)	0
	1001–2000	4 (13%)	0
	2001–3000	6 (20%)	1 (3%)
	3001–4000	3 (10%)	1 (3%)
	>4000	0	0
Increasing trend of β-hCG between Day-4 & Day-7	<1000	0	0
	1001–2000	0	0
	2001–3000	0	3 (10%)
	3001–4000	0	5 (17%)
	>4000	0	2 (7%)
Decreasing trend of β-hCG between Day-4 & Day-7	<1000	3 (10%)	0
	1001–2000	4 (13%)	0
	2001–3000	7 (23%)	0
	3001–4000	3 (10%)	3 (10%)
	>4000	0	0
Relationship between trends on Days 0–4 and 4–7	Increasing Day-4 & Increasing Day-7	0	8 (27%)
	Increasing Day-4 & Decreasing Day-7	1 (3%)	3 (10%)
	Decreasing Day-4 & Increasing Day-7	0	2 (7%)
	Decreasing Day-4 & Decreasing Day-7	16 (53%)	0

In Group A, the majority of patients (94.1%) showed a decrease in β-hCG between days 1–4, with 100% continuing to decrease by day 7. In contrast, Group B showed a majority of patients (84.6%) with increasing β-hCG between days 1–4 and 76.9% with continued increase by day 7 [Table 5].

Table 5: Comparison of β-hCG trends and treatment outcomes between the groups

Variable	Group A (n = 17)	Group B (n = 13)
Treatment outcome	17 (100%)	13 (100%)
Mean β-hCG (mIU/mL)		
Initial (Day-1)	2075.59 ± 981.66	3581.69 ± 503.35
Day-4	1130.18 ± 723.48	3673.54 ± 634.91
Day-7	550.88 ± 593.49	4046.46 ± 674.04
β-hCG trend Day-1 to Day-4		
Increasing	1 (5.88%)	11 (84.62%)
Decreasing	16 (94.12%)	2 (15.38%)
β-hCG trend Day-4 to Day-7		
Increasing	0	10 (76.92%)
Decreasing	17 (100%)	3 (23.08%)
Combined β-hCG trend patterns		
Increasing D1–4 & Increasing D4–7	0	8 (61.54%)
Increasing D1–4 & Decreasing D4–7	1 (5.88%)	3 (23.08%)
Decreasing D1–4 & Increasing D4–7	0	2 (15.38%)
Decreasing D1–4 & Decreasing D4–7	16 (94.12%)	0

DISCUSSION

This study evaluated whether baseline β-hCG and early post-treatment β-hCG trends predict single-dose methotrexate success in tubal ectopic gestation. Our study showed that the success of single-dose methotrexate depends mainly on baseline β-hCG level, gestational sac size, and early decline in β-hCG after treatment. Lower initial β-hCG values and smaller sac dimensions were associated with higher success, and a measurable fall in β-hCG during the first week served as a strong indicator of treatment response. These findings support early identification and selection of suitable candidates for medical management.

Reduced pretreatment β-hCG levels remain the strongest predictor of methotrexate success. Ray et al. identified a β-hCG cut-off of 4,000 mIU/mL with high sensitivity and specificity, and also showed that significant declines in β-hCG on Day-4 and Day-7 predicted successful treatment.[15] Previous studies consistently show that lower baseline β-hCG improves methotrexate success. Our results also reported as individuals who responded to single-dose therapy had notably lower Day-1 β-hCG values. This supported by Tawfiq et al., who reported a 65% failure rate when β-hCG exceeded 4,000 IU/L, compared to only 7.5% when values remained below.[16]

Cohen et al. observed declining success rates as β-hCG levels increased, especially > 4,500 mIU/mL, which is consistent with our finding of reduced success at higher biochemical ranges.[17] Further supported Kirchner who identified serum β-hCG as the most reliable marker, with high response rates when levels were < 10,000 mIU/mL.[18] Cho et al.,

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who demonstrated that when baseline β-hCG was < 6,000 IU/mL, repeat-dose therapy achieved a 96% success rate, while levels > 6,000 significantly reduced treatment success.[19] Although Keikha et al. reported that methotrexate may remain effective at higher β-hCG levels when adjusted or double-dose protocols are used, the prevailing evidence, including our findings, supports improved outcomes with lower biochemical burden.[20]

Ultrasound features such as sac size influence treatment success. Gestational sac size demonstrated parallel predictive value. Kimiaei et al. found that sac sizes > 3 cm were strongly associated with methotrexate failure, and this pattern was evident in our study, where sacs >3 cm rarely responded to treatment.[21] In contrast, sac sizes < 2 cm showed excellent response rates, aligning with the findings of Scarpelli et al., who reported significantly improved outcomes when sac width was <2 cm.[22] Evidence from Mitsui et al. showed improved treatment response when sac size was <10.4 mm and initial β-hCG was <17,757 mIU/mL,[23] supporting the principle that both biochemical and structural disease burden influence treatment success.

Dynamic monitoring of β-hCG following methotrexate administration offers valuable early prognostic insight. As reported by Ray et al., a significant decline in β-hCG by Day 4 and Day 7 strongly predicts therapeutic success. In our study, failure to achieve a ≥ 15% β-hCG decrease within one week similarly portended methotrexate resistance and the need for surgical intervention.[15] Moreover, Chitzios et al. demonstrated that a reduction in gestational sac size together with falling β-hCG levels correlated with favorable outcomes, underscoring the importance of serial assessments rather than relying exclusively on baseline parameters.[24]

Across multiple studies reported patients initial β-hCG levels are < 4,000 mIU/mL, whose gestational sac measures < 2 cm, and who show at least a 15% drop in β-hCG within seven days have the highest likelihood of successful single-dose methotrexate therapy. An initial β-hCG > 4,000–4,500 mIU/mL or a sac size > 3 cm has been associated with increased risk of treatment failure, need for repeat dosing, or surgical management. Our data align closely with these published observations, supporting the practical uses of this quantitative cut-off to improve patient selection, guide medical management, and improve clinical outcomes in the management of ectopic pregnancy.

The prospective study design and scheduled β-hCG measurements allowed a more dependable evaluation of treatment response. Consistent follow-up criteria supported accurate identification of success or resistance. Further larger, multicentre cohorts is needed to confirm these cut-offs in various clinical settings. Comparative research on single-dose, multi-dose, and protocol-adjusted methotrexate based on initial β-hCG level and sac size could help improve patient-specific treatment strategies in ectopic pregnancy.

Limitations: This study is limited by its small sample size and single-centre setting, which may restrict generalisability. Monitoring was limited to Day-7 β-hCG, and factors such as tubal pathology and methotrexate pharmacodynamics were not assessed, and long-term fertility outcomes were not evaluated.

CONCLUSION

Single-dose methotrexate is effective in selected cases of unruptured tubal ectopic pregnancy, with treatment success strongly associated with lower initial β-hCG levels and a declining between Day 0 and Day 4. In contrast, higher baseline β-hCG, particularly > 3000 mIU/mL, and an early increasing predict treatment failure. This shows the importance of early β-hCG monitoring, with Day 4 for evaluating response and guiding timely interventions, such as a second dose.

REFERENCES

1. Coste J, Bouyer J, Job-Spira N. Epidemiology of ectopic pregnancy: incidence and risk factors. Contracept Fertil Sex 1996;24:135–9. https://pubmed.ncbi.nlm.nih.gov/8611934/
2. Lozeau AM, Potter B. Diagnosis and management of ectopic pregnancy. Am Fam Physician 2005;72:1707–14. https://pubmed.ncbi.nlm.nih.gov/16300032/
3. Chang J, Elam-Evans LD, Berg CJ, Herndon J, Flowers L, Seed K, et al. Pregnancy-related mortality surveillance United States, 1991–1999. MMWR Surveill Summ 2003;52:1–8. https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5202a1.htm
4. Wang R, Reynolds TA, West HH, Ravikumar D, Martinez C, McAlpine I, et al. Use of a β-hCG discriminatory zone with bedside pelvic ultrasonography. Ann Emerg Med 2011;58:12–20. https://doi.org/10.1016/j.annemergmed.2010.12.023.
5. Gullo G, Satullo M, Conti E, Ganduscio S, Chitoran E, Kozinszky Z, et al. Gestational trophoblastic disease: Diagnostic and therapeutic updates in light of recent evidence: A literature review. Medicina (Kaunas) 2025;61:1642. https://doi.org/10.3390/medicina61091642.
6. Practice Committee of American Society for Reproductive Medicine. Medical treatment of ectopic pregnancy: a committee opinion. Fertil Steril 2013;100:638–44. https://doi.org/10.1016/j.fertnstert.2013.06.013.
7. Prabhakaran M, Beesetty A. Ectopic pregnancy with low beta-human chorionic gonadotropin (HCG) managed with methotrexate and progressed to rupture. Cureus 2021;13:e18749. https://doi.org/10.7759/cureus.18749.
8. Var A, Özyurt R, Şık BA, Kumbasar S, Sever E, Deveci M, et al. Retrospective analysis of factors that affect the success of single-dose methotrexate treatment in ectopic pregnancy. J Turk Soc Obstet Gynecol 2015;12:215–9. https://doi.org/10.4274/tjod.10576.
9. Hajenius PJ, Mol F, Mol BWJ, Bossuyt PMM, Ankum WM, Van der Veen F. Interventions for tubal ectopic pregnancy. Cochrane Libr 2007. https://doi.org/10.1002/14651858.cd000324.pub2.
10. Stovall TG, Ling FW. Single-dose methotrexate: An expanded clinical trial. Am J Obstet Gynecol 1993;168:1759–65. https://doi.org/10.1016/0002-9378(93)90687-e.
11. Canis M, Savary D, Pouly JL, Wattiez A, Mage G. Ectopic pregnancy: criteria to decide between medical and conservative surgical treatment? J Gynecol Obstet Biol Reprod (Paris). 2003;32:S54–63. https://pubmed.ncbi.nlm.nih.gov/14699319/

ISSN (O): 2687-5365; ISSN (P): 2753-6556

12. Potter MB, Lepine LA, Jamieson DJ. Predictors of success with methotrexate treatment of tubal ectopic pregnancy at Grady Memorial Hospital. Am J Obstet Gynecol 2003;188:1192–4. https://doi.org/10.1067/mob.2003.310.
13. Nazac A, Gervaise A, Bouyer J, De Tayrac R, Capella-Allouc S, Fernandez H. Predictors of success in methotrexate treatment of women with unruptured tubal pregnancies. Ultrasound Obstet Gynecol 2003;21:181–5. https://doi.org/10.1002/uog.9.
14. Dilbaz S, Caliskan E, Dilbaz B, Degirmenci O, Haberal A. Predictors of methotrexate treatment failure in ectopic pregnancy. J Reprod Med 2006;51:87–93. https://europepmc.org/article/med/16572908.
15. Ray A, Gaur A, Kumari S. Predictors of successful medical management with methotrexate in unruptured tubal ectopic pregnancy. Cureus 2022. https://doi.org/10.7759/cureus.31923.
16. Tawfiq A, Agameya A-F, Claman P. Predictors of treatment failure for ectopic pregnancy treated with single-dose methotrexate. Fertil Steril 2000;74:877–80. https://doi.org/10.1016/s0015-0282(00)01547-8.
17. Cohen A, Zakar L, Gil Y, Amer-Alshiek J, Bibi G, Almog B, et al. Methotrexate success rates in progressing ectopic pregnancies: a reappraisal. Am J Obstet Gynecol 2014;211:128.e1-5. https://doi.org/10.1016/j.ajog.2014.03.043.
18. Kirchner DO. Methotrexate in the Treatment of Ectopic Pregnancy. Am Fam Physician 2000;61:2228–9. https://www.aafp.org/pubs/afp/issues/2000/0401/p2228.html.
19. Cho GJ, Lee SH, Shin JW, Lee NW, Kim T, Kim HJ, et al. Predictors of success of repeated injections of single-dose methotrexate regimen for tubal ectopic pregnancy. J Korean Med Sci 2006;21:86. https://doi.org/10.3346/jkms.2006.21.1.86.
20. Keikha F, Ardekani SS, Parsaei M, Zargarzadeh N, Hadizadeh A, Tarafdari A. Methotrexate as the first-line treatment of unruptured tubular ectopic pregnancies with high initial human chorionic gonadotropin levels: A retrospective cohort. Eur J Obstet Gynecol Reprod Biol X 2024;21:100286. https://doi.org/10.1016/j.eurox.2024.100286.
21. Kimiaei P, Khani Z, Marefian A, Gholampour Ghavamabadi M, Salimnejad M. The importance of gestational sac size of ectopic pregnancy in response to single-dose methotrexate. ISRN Obstet Gynecol 2013;2013:269425. https://doi.org/10.1155/2013/269425.
22. Scarpelli E, Capozzi VA, Roberto L, Gallinelli A, Pezzani A, Monica M, et al. Predictors of Methotrexate success and fertility outcomes in tubal ectopic pregnancy: A retrospective cohort study. Medicina (Kaunas) 2025;61:1058. https://doi.org/10.3390/medicina61061058.
23. Mitsui T, Mishima S, Ohira A, Tani K, Maki J, Eto E, et al. hCG values and gestational sac size as indicators of successful systemic methotrexate treatment in cesarean scar pregnancy. Taiwan J Obstet Gynecol 2021;60:454–7. https://doi.org/10.1016/j.tjog.2021.03.011.
24. Chitzios D, Balaouras D, Papasozomenou P, Balaouras G, Mikos T, Daniilidis A, et al. Sonographic vascularity indices' study in ectopic pregnancies, after methotrexate treatment. Eur J Obstet Gynecol Reprod Biol X 2024;22:100316. https://doi.org/10.1016/j.eurox.2024.100316.

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