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Original Research

Effect of Diagnostic Curettage on the Outcome of Medical Treatment for Tubal Pregnancy

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Abstract

Background: Tubal pregnancy, the most common ectopic type, requires urgent intervention. While medical therapy preserves fertility, diagnostic curettage (D&C) is often used if imaging is inconclusive. While medical therapy preserves fertility, D&C is often used if imaging is inconclusive. **Methods**: A retrospective cohort study was conducted to analyze the clinical data of patients with tubal pregnancies who were hospitalized at the First Affiliated Hospital of Guangzhou University of Chinese Medicine, from 2017 to 2021. Univariate analysis and multivariate logistic regression were used to adjust for confounding factors. A subgroup analysis stratified by human chorionic gonadotropin (hCG) level was also performed to investigate the impact of D&C on treatment outcomes. **Results**: The overall failure rate of medical treatment was 24.39% (90/369), with 40.00% (36/90) in the curettage group and 19.35% (54/279) in the control group, showing a significant difference ($p < 0.001$). After adjusting for confounding factors, logistic regression indicated that the curettage group had a significantly higher failure rate of medical treatment compared to the control group ($p = 0.012$), with an adjusted odds ratio (OR) of 2.261 (95% confidence interval [CI]: 1.193–4.283). In other words, patients with tubal pregnancy who underwent curettage had a 2.261-fold higher risk of treatment failure compared to those who did not. In subgroup analysis, among patients with serum hCG $\leq$2000 IU/L, the curettage group had a significantly higher treatment failure rate than the control group (adjusted OR [95% CI] = 2.856 [1.388–5.875], $p = 0.004$). However, no significant difference was observed among patients with serum hCG $>$2000 IU/L ($p > 0.05$). **Conclusion**: D&C may increase the risk of medical treatment failure in patients with tubal pregnancy and serum hCG levels $\leq$2000 IU/L.

Keywords: diagnostic curettage; tubal pregnancy; medical treatment outcome

1. Introduction

Ectopic pregnancy is defined as an abnormal pregnancy in which the fertilized ovum implants outside the uterine cavity. Among all ectopic pregnancies, tubal pregnancy (TP) is the most common, accounting for over 90%. When tubal pregnancy is complicated by rupture and hemorrhage, it can lead to hemorrhagic shock and potentially fatal outcomes, making prompt intervention critical. Medical therapy is a conservative treatment option for tubal pregnancy, offering advantages of being non-invasiveness, reduced pelvic adhesions, and preservation of the affected fallopian tube [1,2]. The expanding role of medical treatment is partly due to improvements in early recognition and diagnosis of ectopic pregnancy. Diagnostic curettage (D&C) is frequently employed as a supplemental diagnostic tool for early ectopic pregnancy. Although ultrasound can diagnose the majority of ectopic pregnancies, D&C remains particularly valuable when imaging results are inconclusive. By examining uterine contents obtained via D&C, clinicians can distinguish ectopic pregnancy from intrauterine pregnancy, thus avoiding misdiagnosis and inappropriate use of medications such as methotrexate [3]. However, despite its diagnostic utility, the invasive nature of D&C raises concerns about its potential interference with efficacy of medical treatment. Early medical treatment for tubal pregnancy offers several advantages, including preservation of the affected fallopian tube, reduction of pelvic adhesions, avoidance of surgical trauma, and decreased treatment costs. This approach also optimizes the pelvic environment and helps maintain future fertility for patients who wish to conceive again [1,2]. Although integrated traditional Chinese and Western medicine has proven effective in appropriately selected patients [4,5], some tubal pregnancy patients still fail to respond to medical therapy and require surgical intervention. Therefore, early assessment of the condition and avoidance of high-risk factors are critically important in the medical management of tubal pregnancy. Diagnostic curettage is widely used as an adjunct tool to distinguish early pregnancies of unknown location. By analyzing pathological findings from endometrial tissue and post-procedure changes in specific serum beta human chorionic gonadotropin (β-hCG) levels, clinicians can rule out normal intrauterine pregnancy and effectively manage conditions such as early miscarriage or hydatidiform mole. Nevertheless, as an invasive procedure, diagnostic curettage carries certain risks of infection and bleeding and is not

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recommended as a routine diagnostic method. The decision of whether to perform curettage in patients with suspected ectopic pregnancy is a key clinical issue addressed in this study. Existing literature focuses predominantly on diagnostic accuracy, while the impact of D&C on pharmacological outcomes—especially in patients eligible for conservative therapy—remains underexplored. This gap is clinically significant, as unnecessary D&C may delay treatment, compromise fertility preservation, or exacerbate treatment failure rates.

In this study, we focused on patients with tubal pregnancy who met the pharmacological treatment criteria described in the Guidelines for Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Tubal Pregnancy [6], using treatment outcomes as the primary measure. The objective was to elucidate the impact of D&C on the medical management of tubal pregnancy and provide clinical guidance for optimizing therapeutic strategies.

2. Materials and Methods

2.1 Study Population

A retrospective cohort study was conducted on patients with tubal pregnancy who received integrated traditional Chinese and Western medicine in the gynecology ward of the First Affiliated Hospital of Guangzhou University of Chinese Medicine from January 2017 to December 2021. Clinical data were retrieved from the hospital's medical record system. Patients were divided into a curettage group (drug treatment plan with diagnostic curettage) and a control group (drug treatment without diagnostic curettage) based on whether they underwent diagnostic curettage during hospitalization. All included patients gave informed consent for the treatment plan and signed the informed consent form for drug treatment of tubal pregnancy. This study was approved by the hospital ethics committee (ethical approval number: JY [2021] 099).

2.1.1 Inclusion Criteria

(1) Women aged 18–45 years, diagnosed with ectopic pregnancy and showing an adnexal mass on color Doppler ultrasound.

(2) Met the criteria for drug therapy specified in the Guidelines for the Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Tubal Pregnancy, including stable vital signs, no signs of tubal rupture, absence of active bleeding, β-hCG levels below the defined threshold, and imaging evidence of a non-ruptured ectopic mass without fetal cardiac activity, and having received at least 5 days of drug therapy.

(3) Had a definitive treatment outcome.

2.1.2 Exclusion Criteria

(1) Pathology confirming ovarian, interstitial or other non-tubal pregnancy.

(2) β-hCG decreased by $\geq$50% every 24 hours without treatment or had already returned to negative.

(3) Concomitant abnormal liver or kidney function; endocrine disorders such as thyroid disease or diabetes; hematologic disorders; infectious diseases; or malignancies.

(4) Missing critical indicators or data.

(5) Did not meet surgical indications during therapy, but opted to terminate drug treatment for personal reasons and underwent surgery.

(6) Did not meet the discharge criteria yet requested discharge, or failed to follow up on β-hCG after discharge, resulting in an unclear outcome.

2.2 Observational Indicators

2.2.1 Drug Treatment Indications

The indications for drug therapy were based on clinical guidelines [6].

(a) Previously positive β-hCG that has become negative, with a tubal pregnancy factor score (Table 1, Ref. [6,7]) $\leq$10 points.

(b) For cases with β-hCG $<$8000 IU/L:

(1) Unruptured stage (no rupture or miscarriage): score $\leq$10 points.

(2) Ruptured stage (tubal rupture or miscarriage): score $\leq$9 points.

Under these conditions, patients are eligible for drug therapy:

(1) For β-hCG $<$1000 IU/L and an unruptured-stage score $\leq$8 points, with tubal mass diameter $\leq$3 cm, or a ruptured-stage score $\leq$9 points, traditional Chinese medicine alone can be used.

(2) For an unruptured-stage score of 9–10 points, or a score $\leq$8 points but β-hCG $\geq$1000 IU/L and tubal mass diameter between 3 cm and 5 cm, and for ruptured-stage patients with β-hCG $\geq$1000 IU/L and a score $\leq$9 points, an integrated traditional Chinese and Western medicine approach is used.

2.2.2 Drug Treatment Plan

2.2.2.1 Traditional Chinese Medicine (TCM). According to the tubal pregnancy factor scoring model, blood β-hCG levels, tubal mass size, and TCM syndrome differentiation based on stage and type of tubal pregnancy [6–8], treatments include a modified ectopic pregnancy formula I (Composition of Chinese medicine soup: Salviae Miltiorrhizae 15 g, Radix Paeoniae Lactiflorae 15 g, Peach Kernel 9 g. Mode of administration of the drug: Oral) or II prescription (Composition of Chinese medicine soup: Salvia miltiorrhiza 15 g, Radix Paeonia lactiflora 15 g, peach kernel 15 g, Mitsubishi 10 g, Curcuma longa 10 g. Mode of administration of the drug: Oral), Huayu Xiaozheng Granules (The First Affiliated Hospital of Guangzhou University of Chinese medicine; Z20170001; Guangzhou, Guangdong, China), Sanjie Zhentong Capsules (Jiangsu

Table 1. Score of influencing factors of tubal pregnancy.

	1 point	2 point	3 point
Gestational weeks	≤6 (weeks)	>6–8 (weeks)	>8 (weeks)
Abnormal pain	Painless	Dull pain	Acute pain
β-hCG	<1000 IU/L	1000–3000 IU/L	>3000 IU/L
Maximum diameter of pelvic hemorrhage (Ultrasonic diagnosis)	<3 cm	3–6 cm	>6 cm
Maximum diameter of tubal pregnancy mass (Ultrasonic diagnosis)	<3 cm	3–5 cm	>5 cm

After adding each item' scores according to the actual situation of the patient, the total score is obtained.

β-hCG, specific serum beta human chorionic gonadotropin.

Kangyuan Pharmaceutical Co.; Z20030127; Lianyungang, Jiangsu, China), Xuefu Zhuyu Granules (Inner Mongolia Kang En Bei Pharmaceutical Co.; Z20050019; Ordos, Inner Mongolia Autonomous Region, China), or Dahuang Zhechong Pills (Shaanxi Hanwang Pharmaceutical Co.; batch number: 1907701; Hanzhong, Shaanxi, China. Mode of administration of the drug: Oral), in addition to Shuangbai Powder (Composition of traditional chinese medicine powder: Rhubarb 60 g, platycladus orientalis leaves 60 g, Eupatorium 30 g, Mentha haplocalyx 30 g, Phellodendron chinense Schneid 30 g. Mode of administration of the drug: applied externally on the lower abdomen).

2.2.2.2 Western Medicine. Single, double, or multi-dose regimens of methotrexate (MTX; Zhejiang Hai Zheng Pharmaceutical Co.; H20055198; Taizhou, Zhejiang, China. Mode of administration of the drug: intramuscular injection, 50 mg/m^2), and mifepristone (Zhejiang Xianju Pharmaceutical Sales Co., Ltd.; H10950347; Hangzhou, Zhejiang, China. Mode of administration of the drug: Oral) alone or in combination with MTX.

2.2.3 Treatment Outcome Criteria

2.2.3.1 Cured Group. Patients were classified as "Cured" if their blood β-hCG levels decreased consistently during treatment and fell below 10 IU/L at discharge, regardless of whether diagnostic curettage was performed.

2.2.3.2 Accepted Surgery Group. Patients were classified as "Accepted surgery" if they met any of the following criteria for treatment failure: (1) rising β-hCG levels; (2) onset or worsening of abdominal pain; (3) detection of fetal cardiac activity in the adnexal mass; (4) suspected tubal rupture with hemorrhage; or (5) progressive pelvic bleeding requiring surgical intervention (laparoscopy/laparotomy), excluding cases of elective surgery for personal reasons.

2.2.4 Confounding Factor Control

Based on previous studies examining factors influencing ectopic pregnancy drug treatment outcomes [9,10] and tubal pregnancy rupture [11–14], potential confounding variables included:

(1) Pregnancy Variables: Duration of amenorrhea, gestational weeks, pretreatment blood β-hCG, and progesterone levels.

(2) Clinical Symptoms: Abdominal pain, presence or absence of vaginal bleeding.

(3) Medical History: Previous ectopic pregnancy, number of abortions, history of tubal surgery.

(4) Ultrasound Findings: Location of the tubal pregnancy, extent of pelvic effusion, diameter of the pregnancy mass, and endometrial thickness.

(5) Drug Treatment Regimen: Type of pharmacological therapy received.

2.3 Statistical Methods

All statistical analyses were performed using the EmpowerStats software (http://www.empowerstats.com, X&YSolutions, Inc., Boston, MA, USA) based on the R language. First, univariate analysis was conducted to identify potential confounding factors influencing treatment outcome. The Kolmogorov-Smirnov test (SPSS 25.0, IBM Corp., Armonk, NY, USA) was used to assess the normality of continuous data. For non-normally distributed variables, the median (lower quartile, upper quartile) was used for description, and the Mann-Whitney U test was used for comparison between groups. Categorical data were expressed as frequency (percentage) and compared using the Pearson chi-square test. Subsequently, multivariate logistic regression analysis was performed to adjust for confounding factors and assess the impact of diagnostic curettage on tubal pregnancy treatment outcomes. A significance level of $p < 0.05$ was used for all statistical tests.

3. Results

3.1 Baseline Characteristic of Participants

A total of 369 eligible patients were included in this study and categorized into two mutually exclusive outcome groups based on predefined criteria (see Section 2.2.3). Cured group (n = 279): Patients who achieved successful medical treatment outcomes (β-hCG <10 IU/L at discharge). Accepted surgery group (n = 90): Patients who required surgical intervention due to treatment failure. The overall treatment failure rate was 24.39% (90/369). From the entire cohort of 369 participants, the 90 patients who underwent diagnostic curettage were assigned to the curettage group. The cohort was divided into two mutually exclusive groups based on therapeutic protocol. Curettage group (n = 90): Patients who underwent diagnostic curet-

tage prior to combined therapy. Within this subgroup, 36 cases (40.00%) ultimately required surgery due to treatment failure. Control group (n = 279): Patients treated with medication alone. Among these, 54 cases (19.35%) failed to respond and required surgical intervention. The overall treatment failure rate was 24.39% (90/369), derived from the sum of failures in both groups (54 + 36). A statistically significant difference in failure rates was observed between the curettage group and the control group (40.00% *vs.* 19.35%, $p < 0.001$). Importantly, all baseline characteristics (e.g., vaginal bleeding, hCG levels) were adjusted in multivariable analyses to ensure the robustness of this association.

During the same period, only 8 patients suspected of ectopic pregnancy were ultimately diagnosed with intrauterine pregnancy via diagnostic curettage (these cases were excluded from the study). In addition, there were also statistically significant differences between the curettage and control groups in terms of vaginal bleeding symptoms, blood hCG levels, the "hCG value/days of amenorrhea" ratio, progesterone levels, endometrial thickness, and treatment regimen (all $p < 0.05$) (Table 2). By contrast, factors such as duration of amenorrhea, abdominal pain, and the diameter of the pregnancy mass did not differ significantly between the 2 groups ($p > 0.05$).

3.2 Univariate Analysis Results

Through univariate analysis to explore the impact of various indicators on the drug treatment outcome, the results demonstrated that the days of amenorrhea, weeks of amenorrhea, number of abortions, history of ectopic pregnancy, history of tubal surgery, blood hCG value, "blood hCG value/days of amenorrhea" ratio, progesterone value, diameter of the pregnancy mass, endometrial thickness, drug treatment plan, and diagnostic curettage operation were related to the drug treatment outcome, with statistically significant differences ($p < 0.05$), while other factors such as abdominal pain, vaginal bleeding symptoms, and range of pelvic effusion had no statistically significant impact on the drug treatment outcome ($p > 0.05$) (Table 3).

3.3 Multivariate Logistic Regression Analysis

To further evaluate the effect of diagnostic curettage on the outcome of drug therapy for tubal pregnancy, we performed multivariate logistic regression after adjusting for the confounding factors previously identified. In addition, given the substantial influence of blood hCG levels on treatment outcomes, a subgroup analysis was conducted using 2000 IU/L as the cutoff. The results are presented in Fig. 1. Overall, a significant difference in treatment outcomes was observed between the curettage group and the control group ($p = 0.012$), with an OR (95% CI) of 2.261 (1.193–4.283), indicating that the failure probability of tubal pregnancy patients who underwent curettage during treatment was 2.261 times (1.193, 4.283) that of those who did not. In the subgroup with blood β-hCG $\leq$2000 IU/L, diagnostic curettage had a marked impact on outcomes ($p = 0.004$), with an OR (95% CI) of 2.856 (1.388–5.875). Hence, the failure risk for patients with β-hCG $\leq$2000 IU/L who underwent curettage was 2.856 times that of those who did not. Conversely, in the subgroup with β-hCG >2000 IU/L, diagnostic curettage did not significantly affect treatment outcomes ($p > 0.05$).

4. Discussion

This study evaluated the impact of diagnostic curettage on the outcomes of medical treatment for tubal pregnancy in a cohort of 369 patients. We found that patients who underwent diagnostic curettage had a significantly higher rate of treatment failure compared to those who did not. After adjusting for relevant confounding factors, diagnostic curettage was associated with a more than twofold increase in the odds of treatment failure. Notably, in the subgroup of patients with β-hCG levels $\leq$2000 IU/L, the risk was nearly threefold higher, whereas no significant difference was observed in patients with β-hCG >2000 IU/L. These findings suggest that diagnostic curettage may adversely affect medical treatment efficacy, particularly in patients with lower β-hCG levels. Compared with the control group, the curettage group had significantly higher median values of endometrial thickness (11.0 mm), blood β-hCG value (1545.5 IU/L), "hCG value/days of amenorrhea" ratio (14.55 IU/L/d), and progesterone value (19.19 nmol/L), indicating that patients with thicker endometrium, higher blood β-hCG value, and higher progesterone value are more likely to undergo diagnostic curettage to exclude intrauterine pregnancy in clinical practice. Due to the limited development of trophoblast cells in tubal pregnancy, insufficient secretion of β-hCG, reduced progesterone secretion by the corpus luteum, delayed endometrial decidualization, endometrial thickness, blood β-hCG value, and progesterone value have certain reference values for differentiating between intrauterine and ectopic pregnancies [15–19]. Thus, endometrial thickness, blood β-hCG level, and progesterone level are important indicators that guide clinicians when deciding whether to perform diagnostic curettage. However, no clear consensus exists regarding threshold values for these parameters in the early diagnosis of ectopic pregnancy. Several studies report that mean endometrial thickness is 6–8 mm in ectopic pregnancy at 5–8 weeks of gestation, whereas it is 11–12 mm in normal intrauterine pregnancy [15–18]. Taking 11–12 mm as a reference, patients with an endometrial thickness in this range often undergo diagnostic curettage if intrauterine pregnancy cannot be definitively ruled out. In addition, assessing blood β-hCG and progesterone levels is crucial for early diagnosis of ectopic pregnancy. In clinical practice, serum β-hCG levels and their dynamic changes play a critical role in evaluating pregnancies of unknown location. A study [15] suggests that when β-hCG levels are below 2000 IU/L and no intrauterine gestational sac is visualized on ultrasound, the diagnostic rate for ectopic preg-

Table 2. Basic characteristics of patients between D&C group and control group.

Factors	Control group (n = 279)	D&C group (n = 90)	Z/χ^2 value	p value
Duration of amenorrhea (days)	47 (40, 54)	45 (41, 52)	–0.864	0.387
Duration of amenorrhea (weeks)	-	-	3.147	0.207
<6	76 (27.24%)	25 (27.78%)	-	-
6–8	150 (53.76%)	55 (61.11%)	-	-
>8	53 (19.00%)	10 (11.11%)	-	-
Age (year)	30 (26, 33)	31 (27, 36)	1.626	0.104
Pregnant position	-	-	0.026	0.873
Left fallopian tube	136 (48.75%)	43 (47.78%)	-	-
Right fallopian tube	143 (51.25%)	47 (52.22%)	-	-
Abdominal pain	-	-	0.397	0.820
Painless	87 (31.18%)	31 (34.44%)	-	-
Dull pain	107 (38.35%)	34 (37.78%)	-	-
Acute pain	85 (30.47%)	25 (27.78%)	-	-
Vaginal bleeding	-	-	7.918	0.005
No	17 (6.09%)	14 (15.56%)	-	-
Yes	262 (93.91%)	76 (84.44%)	-	-
No. of artificial abortion	-	-	1.409	0.235
0–1	207 (74.19%)	61 (67.78%)	-	-
≥2	72 (25.81%)	29 (32.22%)	-	-
History of ectopic pregnancy	-	-	0.198	0.656
No	232 (83.15%)	73 (81.11%)	-	-
Yes	47 (16.85%)	17 (18.89%)	-	-
Previous tubal surgery	-	-	0.043	0.835
No	233 (83.51%)	76 (84.44%)	-	-
Yes	46 (16.49%)	14 (15.56%)	-	-
Serum β-hCG levels (IU/L)	383.9 (160.2, 1034.0)	1545.5 (767.6, 2154.9)	3.599	<0.001
The ratio of serum hCG level to days of amenorrhea (IU/L/d)	7.91 (3.29, 21.33)	14.55 (8.11, 29.69)	3.676	<0.001
Progesterone levels (nmol/L)	11.38 (4.79, 22.94)	19.19 (10.71, 39.58)	4.639	<0.001
Diameter of gestational mass	-	-	4.737	0.094
<3 cm	170 (60.93%)	66 (73.33%)	-	-
3–5 cm	95 (34.05%)	20 (22.22%)	-	-
>5 cm	14 (5.02%)	4 (4.44%)	-	-
Range of pelvic effusion	-	-	0.287	0.962
0 cm	125 (44.80%)	42 (46.67%)	-	-
<3 cm	43 (15.41%)	12 (13.33%)	-	-
3–6 cm	91 (32.62%)	29 (32.22%)	-	-
>6 cm	20 (7.17%)	7 (7.78%)	-	-
Endometrial thickness (mm)	8.0 (5.4, 11.0)	11.0 (8.0, 15.0)	5.644	<0.001
Medical management	-	-	10.055	0.007
TCM treatment	162 (58.06%)	35 (38.89%)	-	-
TCM and western medicine treatment	83 (29.75%)	39 (43.33%)	-	-
Western medicine was added after TCM treatment	34 (12.19%)	16 (17.78%)	-	-
Treatment outcome	-	-	15.728	<0.001
Cured	225 (80.65%)	54 (60.00%)	-	-
Accepted surgical operation	54 (19.35%)	36 (40.00%)	-	-

Notes: Cured group (n = 279): Patients with successful medical treatment (β-hCG <10 IU/L at discharge). Accepted surgery group (n = 90): Patients requiring surgery due to treatment failure (see Section 2.2.3). D&C, diagnostic curettage; TCM, Traditional Chinese Medicine. The measurement data that do not meet the normal distribution are described by the median (lower quartile, upper quartile), and the counting data are described by the number of cases (percentage). $p < 0.05$ was considered to be statistically significant.

nancy is limited (generally ≤50%). Performing diagnostic curettage at this stage may risk disrupting a potential viable intrauterine pregnancy that is too early to confirm sonographically. Conversely, if β-hCG exceeds 5000 IU/L

Table 3. Univariate analysis of effects on medical treatment outcomes.

Factors	Medical treatment outcomes			
	Cured (n = 279)	Accepted surgery (n = 90)	OR (95% CI)	*p* value*
Duration of amenorrhea (days)	47 (42, 54)	44 (40, 50)	0.98 (0.96, 1.00)	<0.001
Duration of amenorrhea (weeks)	-	-	-	0.026
<6	68 (24.37%)	33 (36.67%)	1.00	-
6–8	157 (56.27%)	48 (53.33%)	0.63 (0.37, 1.07)	0.086
>8	54 (19.35%)	9 (10.00%)	0.34 (0.15, 0.78)	0.011
Pregnant position	-	-	-	-
Left fallopian tube	131 (46.95%)	48 (53.33%)	1.00	-
Right fallopian tube	148 (53.05%)	42 (46.67%)	0.77 (0.48, 1.25)	0.352
Abdominal pain	-	-	-	0.825
Painless	91 (32.62%)	27 (30.00%)	1.00	-
Dull pain	107 (38.35%)	34 (37.78%)	1.07 (0.60, 1.91)	0.816
Acute pain	81 (29.03%)	29 (32.22%)	1.21 (0.66, 2.21)	0.542
Vaginal bleeding	-	-	-	-
No	23 (8.24%)	8 (8.89%)	1.00	-
Yes	256 (91.76%)	82 (91.11%)	0.92 (0.40, 2.14)	1.000
No. of artificial abortion	-	-	-	-
0–1	215 (77.06%)	53 (58.89%)	1.00	-
≥2	64 (22.94%)	37 (41.11%)	2.35 (1.42, 3.88)	0.001
History of ectopic pregnancy	-	-	-	-
No	238 (85.30%)	67 (74.44%)	1.00	-
Yes	41 (14.70%)	23 (25.56%)	1.99 (1.12, 3.55)	0.027
Previous tubal surgery	-	-	-	-
No	243 (87.10%)	66 (73.33%)	1.00	-
Yes	36 (12.90%)	24 (26.67%)	2.45 (1.37, 4.40)	0.004
Serum β-hCG levels (IU/L)	373.0 (149.6, 800.5)	1264.0 (438.4, 2484.0)	1.00 (1.00, 1.00)	<0.001
The ratio of serum hCG level to days of amenorrhea (IU/L/d)	7.89 (3.24, 16.86)	30.17 (9.00, 54.58)	1.03 (1.02, 1.05)	<0.001
Progesterone levels (nmol/L)	11.30 (4.87, 22.00)	22.31 (11.16, 37.87)	1.02 (1.01, 1.03)	<0.001
Diameter of gestational mass	-	-	-	0.007
<3 cm	166 (59.50%)	70 (77.78%)	1.00	-
3–5 cm	97 (34.77%)	18 (20.00%)	0.44 (0.25, 0.78)	0.005
>5 cm	16 (5.73%)	2 (2.22%)	0.30 (0.07, 1.32)	0.111
Range of pelvic effusion	-	-	-	0.875
0 cm	124 (44.44%)	43 (47.78%)	1.00	-
<3 cm	42 (15.05%)	13 (14.44%)	0.89 (0.44, 1.82)	0.754
3–6 cm	91 (32.62%)	29 (32.22%)	0.92 (0.53, 1.58)	0.761
>6 cm	22 (7.89%)	5 (5.56%)	0.66 (0.23, 1.84)	0.422
Endometrial thickness (mm)	8.0 (6.0, 12.0)	10.0 (6.63, 13.0)	1.08 (1.03, 1.13)	<0.001
Medical management	-	-	-	<0.001
TCM treatment	170 (60.93%)	27 (30.00%)	1.00	-
TCM and western medicine treatment	68 (24.37%)	54 (60.00%)	5.00 (2.91, 8.59)	<0.001
Western medicine was added after TCM treatment	41 (14.70%)	9 (10.00%)	1.38 (0.60, 3.16)	0.444
Diagnostic curettage	-	-	-	-
No	225 (80.65%)	54 (60.00%)	1.00	-
Yes	54 (19.35%)	36 (40.00%)	2.78 (1.66, 4.65)	0.001

Notes: OR, odds ratio; CI, confidence interval. Cured group: Patients with successful medical treatment (β-hCG <10 IU/L at discharge). Accepted surgery group: Patients who failed medical treatment and required surgical intervention (see Section 2.2.3 for criteria). Continuous non-normally distributed data are presented as median (lower quartile, upper quartile); categorical data as frequency (percentage). * refers to the *p* value calculated by continuity correction. $p < 0.05$ was considered that the difference is statistically significant.

without evidence of an intrauterine gestational sac, the likelihood of ectopic pregnancy becomes significantly high (exceeding 90%), rendering diagnostic curettage unnecessary for differential diagnosis. Additionally, serial β-hCG moni-

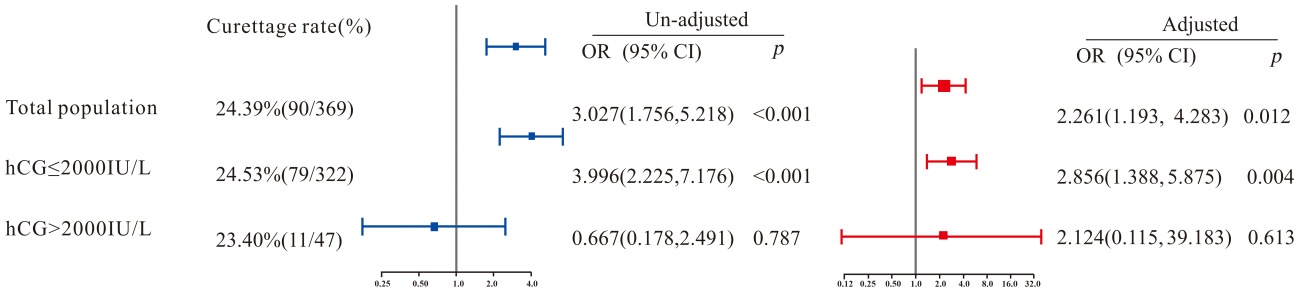

Fig. 1. Multivariate logistic regression on the correlation between diagnostic curettage and medical treatment outcome. OR, odds ratio; CI, confidence interval; hCG, human chorionic gonadotropin.

toring over 48 hours is recommended to assess the rate of increase; a suboptimal rise (<50%) may further support suspicion of ectopic pregnancy or nonviable gestation, guiding clinical decision-making while minimizing invasive interventions. Some scholars believe that the blood β-hCG value should be measured by the percentage increase in 48 hours. If the increase in blood β-HCG value in 48 hours is less than 52.6%, normal intrauterine pregnancy can be basically excluded. In practice, for suspected tubal pregnancy patients with endometrial thickness $\geq$10–11 mm, blood β-hCG value >2000 IU/L and $\leq$5000 IU/L, and progesterone value >5.6 ng/mL but <25 ng/mL, clinicians might perform diagnostic curettage if ectopic pregnancy cannot be confirmed or excluded by ultrasound alone. However, since diagnostic curettage is an invasive uterine cavity operation, it may cause endometrial growth restriction or intrauterine adhesions, and even lead to a decrease in clinical pregnancy rate and infertility [20,21]. Therefore, the patient's fertility goals and personal preferences must be thoroughly considered before recommending diagnostic curettage.

Previous studies have not definitively clarified whether diagnostic curettage influences the outcomes of medical therapy in tubal pregnancy. However, this 5-year retrospective cohort study indicates that, even after controlling for factors such as blood β-hCG levels, progesterone, endometrial thickness, and treatment plan, diagnostic curettage may be an independent risk factor for the failure of drug therapy in tubal pregnancy.

Recognizing the significant role of blood β-hCG levels in treatment outcomes, we conducted a subgroup analysis using 2000 IU/L as a cutoff. In patients with blood β-hCG $\leq$2000 IU/L, the odds of treatment failure among those who underwent curettage were approximately 2–3 times greater than in those who did not, independent of other factors such as endometrial thickness, progesterone level, or treatment plan.

Consequently, clinicians should avoid diagnostic curettage whenever possible in patients with β-hCG $\leq$2000 IU/L who qualify for medical therapy to reduce the likelihood of treatment failure.

The diagnostic curettage operation process includes intravenous anesthesia, curettage operation, and postoperative anti-infection treatment. The use of anesthetic and broad-spectrum antibiotics may inhibit the intestinal flora and affect liver and kidney function to some extent, thereby affecting the absorption and metabolism of drugs and weakening the therapeutic effect of drugs on early tubal pregnancy.

In addition, the curettage operation removes the thick functional layer of the endometrium, which is rich in estrogen and progesterone receptors. This may reduce the local estrogen and progesterone receptors in the endometrium, thereby affecting the regulatory mechanism of estrogen and progesterone and further affecting the progress of early tubal pregnancy.

From the perspective of traditional Chinese medicine, uterine cavity operation damages the blood vessels of the uterus to some extent, causing some blood to overflow outside the vessels. The blood that leaves the meridians is transformed into blood stasis, blocking the uterine vessels and causing qi stagnation in the uterus and Chong and Ren meridians. In addition, there is a deficiency of essence and blood. The kidney governs the uterus and stores essence, and the kidney essence and qi are indirectly damaged, resulting in failure to store essence and the fetus is not restrained, leading to disease progression.

Although the mechanisms remain speculative, the findings of this study warrant clinical attention. Because this was a single-center, retrospective study with a relatively modest sample size, further research in multi-center settings with larger sample sizes is recommended. A future prospective, randomized controlled trial could provide more definitive evidence on whether diagnostic curettage affects the outcomes of drug therapy for tubal pregnancy. Considering comprehensively the auxiliary diagnostic value of diagnostic curettage for tubal pregnancy and its impact on drug treatment, for suspected tubal pregnancy patients with a blood β-hCG value >2000 IU/L and $\leq$5000 IU/L, endometrial thickness $\geq$11 mm, and progesterone value >5.6 ng/mL and <25 ng/mL, diagnostic curettage can be used for auxiliary diagnosis in combination with the patient's fertility requirements and personal wishes. However, for tubal pregnancy patients with a blood β-hCG value $\leq$2000 IU/L who meet the drug treatment indications, curettage

should be avoided as much as possible. Therefore, for those patients, a wait-and-see approach can be a potential option. This approach can reduce the possibility of trauma and infection, avoid the loss of a viable embryo, and reduce the failure rate of drug treatment management. Clinicians should improve other diagnostic methods, such as In hemodynamically stable patients, combining posterior culdocentesis with simultaneous measurement of β-hCG concentrations in serum and peritoneal fluid can improve both the diagnostic accuracy of ectopic pregnancy and the procedural reliability of culdocentesis [22,23]. In addition, it is expected that the sample size can be further increased in the future and multi-hospital and multi-center cooperation can be carried out. If necessary, a prospective randomized controlled trial can be conducted to observe the impact of diagnostic curettage on the outcome of drug treatment for tubal pregnancy to obtain more accurate results. Given the retrospective nature of the data and the limited sample size, we did not perform subgroup analyses to compare the efficacy of each individual treatment modality. Furthermore, treatment decisions were based on clinicians' judgment and patient conditions, making it difficult to ensure balanced group sizes or eliminate potential confounding factors. Nevertheless, we acknowledge that understanding the individual contribution of each treatment would be valuable, especially mifepristone treatment [24], and future prospective studies should address this question in a more controlled setting. Meanwhile, we have considered the role of TCM in the management of tubal pregnancies. Although the current body of high-quality randomized controlled trials remains limited, emerging evidence from clinical studies [4,7] and an evidence-based guideline [6] suggests that certain herbal formulations used in TCM may offer adjunctive benefits. These include promoting the resorption of ectopic gestational tissue, reducing local inflammation, and facilitating the recovery of tubal function following conservative treatment [25,26]. Such effects are thought to be mediated by the pharmacological properties of specific herbs traditionally used to regulate blood flow and resolve stasis [27].

5. Conclusion

In conclusion, our findings indicated that diagnostic curettage may increase the likelihood of medical treatment failure in tubal pregnancy, particularly when blood β-hCG levels were $\leq$2000 IU/L. While curettage remains a valuable diagnostic tool, clinicians should use it sparingly—especially in patients with a strong desire to preserve fertility—to minimize invasive procedures and potential complications.

Availability of Data and Materials

The authors serve as custodians of the anonymized data, which may be made available from the corresponding author upon reasonable request.

Author Contributions

LY and XW performed the research. JQ and CZ provided help and advice on acquisition of data, LY and XW analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was carried out in accordance with the guidelines of the Declaration of Helsinki. The protocol was approved by the Ethics Committee of Guangzhou University of Chinese Medicine (ethical approval number: JY [2021] 099). Written informed consent was obtained from all participants or their legal guardians prior to their inclusion in the study.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Hu C, Chen Z, Hou H, Xiao C, Kong X, Chen Y. Infertility evaluation via laparoscopy and hysteroscopy after conservative treatment for tubal pregnancy. International Journal of Clinical and Experimental Medicine. 2014; 7: 3556–3561.

[2] Lipscomb GH, Givens VM, Meyer NL, Bran D. Comparison of multidose and single-dose methotrexate protocols for the treatment of ectopic pregnancy. American Journal of Obstetrics and Gynecology. 2005; 192: 1844–1847. https://doi.org/10.1016/j.ajog.2004.12.061.

[3] Givens VM, Lipscomb GH. Diagnosis of ectopic pregnancy. Clinical Obstetrics and Gynecology. 2012; 55: 387–394. https://doi.org/10.1097/GRF.0b013e31824e3618.

[4] Wang J, Yang Q, Yu Z. Clinical study of tubal pregnancy treated with integrated traditional Chinese and Western medicine. Chinese Journal of Integrated Traditional and Western Medicine. 1998; 18: 531–533. (In Chinese)

[5] Hajenius PJ, Mol F, Mol BW, Bossuyt PM, Ankum WM, van der Veen F. Interventions for tubal ectopic pregnancy. Cochrane Database of Systematic Reviews. 2007; 2007: CD000324. https://doi.org/10.1002/14651858.CD000324.

[6] Committee of Obstetrics and Gynecology of the Chinese Society of Integrative Medicine. Diagnosis and treatment guidelines of tubal pregnancy by integrative medicine. Chinese Journal of Practical Gynecology and Obstetrics. 2021; 37: 172–180. (In Chinese)

[7] Deng G, He H, He Y. Influence of disease-influencing factors on staged diagnosis and treatment of patients with tubal pregnancy.

Journal of Traditional Chinese Medicine. 2004; 45: 447–449. (In Chinese)

[8] Faraji Darkhaneh R, Asgharnia M, Farahmand Porkar N, Alipoor AA. Predictive value of maternal serum β-hCG concentration in the ruptured tubal ectopic pregnancy. Iranian Journal of Reproductive Medicine. 2015; 13: 101–106.

[9] Vaswani PR. Predictors of success of medical management of ectopic pregnancy in a tertiary care hospital in United arab emirates. Journal of Clinical and Diagnostic Research. 2014; 8: OC04–OC08. https://doi.org/10.7860/JCDR/2014/8152.4712.

[10] Fu L, Liu X, Tian Z, Du Z, Wang X, Wang X, *et al*. Risk factors for methotrexate treatment failure in tubal ectopic pregnancy: a retrospective cohort study. BMC Pregnancy Childbirth. 2024; 24: 884. https://doi.org/10.1186/s12884-024-07122-6.

[11] Xu C, Mao Z, Tan M, Mazhari SA, Ghorbani Vajargah P, Karkhah S, *et al*. Prevalence and related factors of rupture among cases with ectopic pregnancy; a systematic review and meta-analysis. Archives of Academic Emergency Medicine. 2023; 12: e2. https://doi.org/10.22037/aaem.v11i1.2172.

[12] Bonin L, Pedreiro C, Moret S, Chene G, Gaucherand P, Lamblin G. Predictive factors for the methotrexate treatment outcome in ectopic pregnancy: a comparative study of 400 cases. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2017; 208: 23–30. https://doi.org/10.1016/j.ejogrb.2016.11.016.

[13] Fukami T, Tsujioka H, Matsuoka S, Sorano S, Tohyama A, Yamamoto H, *et al*. Rupture risk factors of fallopian tubal pregnancy. Clinical and Experimental Obstetrics & Gynecology. 2016; 43: 800–802.

[14] Xia W, Zhang J, Zhang D, Zhu Q, Zhang H, Huang Z, *et al*. Left-right asymmetry of tubal pregnancy: a 12-year retrospective hospital-based study. Journal of Minimally Invasive Gynecology. 2019; 26: 671–678. https://doi.org/10.1016/j.jmig.2018.07.010.

[15] American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 193: Tubal Ectopic Pregnancy. Obstetrics Gynecology. 2018; 131: e91–e103. https://doi.org/10.1097/AOG.0000000000002560.

[16] Barnhart KT, Sammel MD, Rinaudo PF, Zhou L, Hummel AC, Guo W. Symptomatic patients with an early viable intrauterine pregnancy. Obstetrics & Gynecology. 2004; 104: 50–55. https://doi.org/10.1097/01.AOG.0000128174.48843.12.

[17] Li W, Liu Z, Ma Y, Zhao T, Liu Y, Qin L, *et al*. Diagnostic value of colour Doppler ultrasound, serum β-hCG concentration, and progesterone concentration in ectopic pregnancy. Technology and Health Care. 2025; 33: 789–796. https://doi.org/10.1177/09287329241296379.

[18] Mullany K, Minneci M, Monjazeb R, C. Coiado O. Overview of ectopic pregnancy diagnosis, management, and innovation. Women's Health. 2023; 19: 1–13. https://doi.org/10.1177/17455057231160349.

[19] Zou S, Li X, Feng Y, Sun S, Li J, Egecioglu E, *et al*. Comparison of the diagnostic values of circulating steroid hormones, VEGF-a, PIGF, and ADAM12 in women with ectopic pregnancy. Journal of Translational Medicine. 2013; 11: 44. https://doi.org/10.1186/1479-5876-11-44.

[20] Condous G, Kirk E, Lu C, Van Calster B, Van Huffel S, Timmerman D, *et al*. There is no role for uterine curettage in the contemporary diagnostic workup of women with a pregnancy of unknown location. Human Reproduction. 2006; 21: 2706–2710. https://doi.org/10.1093/humrep/del223.

[21] Hooker AB, Lemmers M, Thurkow AL, Heymans MW, Opmeer BC, Brolmann HAM, *et al*. Systematic review and meta-analysis of intrauterine adhesions after miscarriage: prevalence, risk factors and long-term reproductive outcome. Human Reproduction Update. 2014; 20: 262–278. https://doi.org/10.1093/humupd/dmt045.

[22] DeCherney AH, Jones EE. Ectopic Pregnancy. Clinical Obstetrics and Gynecology. 1985; 28: 365–374.

[23] Lu Q, Wang Y, Sun X, Li Y, Wang J, Zhou Y, *et al*. The diagnostic role of the β-hCG discriminatory zone combined with the endometrial pattern for ectopic pregnancy in Chinese women. Scientific Reports. 2019; 9: 13781. https://doi.org/10.1038/s41598-019-50151-x.

[24] Stabile G, Romano F, Zinicola G, Topouzova GA, Di Lorenzo G, Mangino FP, *et al*. Interstitial ectopic pregnancy: the role of mifepristone in the medical treatment. International Journal of Environmental Research and Public Health. 2021; 18: 9781. https://doi.org/10.3390/ijerph18189781.

[25] Wu Y, Wu Y, Li B, Yan Z. Cryptotanshinone: a review of its pharmacology activities and molecular mechanisms. Fitoterapia. 2020; 145: 104633.

[26] Tan YQ, Chen HW, Li J, Wu QJ. Efficacy, Chemical Constituents, and Pharmacological Actions of *Radix Paeoniae Rubra* and *Radix Paeoniae Alba*. Frontiers in Pharmacology. 2020; 11: 1054. https://doi.org/10.3389/fphar.2020.01054.

[27] Wei B, Sun C, Wan H, Shou Q, Han B, Sheng M, *et al*. Bioactive components and molecular mechanisms of Salvia miltiorrhiza Bunge in promoting blood circulation to remove blood stasis. Journal of Ethnopharmacology. 2023; 317: 116697. https://doi.org/10.1016/j.jep.2023.116697.