CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1494103

Available online at: http://www.iajps.com Research Article

# A COMPARATIVE STUDY ON THE CONSEQUENCES OF EXPECTANT AND MEDICAL MANAGEMENT IN THE PATIENT HAVING UNRUPTURED TUBAL PREGNANCY

**[1]Dr. Arslan Ahmed, [2]Omer Farooq, [3]Javeria Haroon**

[1]Medical Officer THQ Hospital Chowk Azam

[2]Mayo Hospital Lahore

[3]Mayo Hospital Lahore

**Abstract:**

***Objective:*** *The aim of this research is to compare medical and expectant management among the patients who had β-hcg 1000-3000 IU/L of unruptured-tubal pregnancy.*

***Materials & Methods:*** *The number of patients for this study was 82 with 18-40 years' age, who had 1 to 3 thousand IU/L of the β-hcg level of tubal ectopic pregnancy. The study excluded patients with hetero-tropic pregnancy, non-tubal pregnancy, hypersensitivity to methotrexate, and ruptured ectopic. We made two groups (A: Expectant and B: medical management) through the lottery method. According to our research, if the level of β-hcg of a patient is less than 10 IU/L with pelvic-free fluid, adnexal absence, and gestational sac on ultra-sonography, measuring the result after two weeks, the process is successful.*

***Results:*** *The mean age of the women in group A and B was 30.9±5.95 and 30.65±6.37 years respectively. Gestational age (mean) was 07.12±02.12 and 07.63±02.41 weeks among the patients of group A and B respectively. Mean β-hcg level in group A and B was 1584.63 ± 515.81 and 1537.33 ± 519.68 IU/L. The mean β-hcg levels in group A was 1584.63±515.81 and in group, B was 1537.33±519.68 IU/L. The percentage of success in group A was 90.24 and group B was 63.4 with 0.004 p-values.*

***Conclusion:*** *Our study concludes that while dealing with tubal-ectopic pregnancy with β-hcg 1000 to 3000 IU/L, expectant management has more successful results.*

**Keywords:** *Immuno-Assay, Intra-Uterine, Tubal, Fertilized, Expectant, Medical, Ovum, Laparoscopy.*

**Corresponding author:**

**Dr. Arslan Ahmed,**

*Medical Officer,*

*HQ Hospital Chowk Azam*

QR code

*Please cite this article in press Arslan Ahmed et al.,* ***A Comparative Study on the Consequences of Expectant and Medical Management in the Patient Having Unruptured Tubal Pregnancy.,*** *Indo Am. J. P. Sci, 2018; 05(11).*

## INTRODUCTION:

Ectopic pregnancy is a pregnancy with fertilized ovum implanted outside the cavity of uterine [1]. The reason for most of the maternal morbidity/mortality in the 1st trimester is EP with 0.5 to 02% incidence rate globally [2]. EP becomes acute its diagnosis/treatment is delayed. With in-time diagnosis/treatment, the risk of EP is reduced in terms of maternal morbidity/mortality. Bleeding in early pregnancy is a major diagnosis in the exclusion [3]. EPUs (Early Pregnancy Units) can diagnose EP easily with their access to high-resolution TVS (Trans-Vaginal Ultra-sonography) and rapid Immuno-assay of hCG serum. The rate of EP visualization is 90% currently [4]. As a result, EP has become a non-life-threatening condition for a woman having the availability of non-surgical treatment [5]. There also exists a group of women with EP, not needing surgical management. Prevention of injury (iatrogenic) to the Fallopian tubes is one of the potential advantages of treating EP non-surgically. This improves the chances of intra-uterine conception and reduces recurrent EP's risks. With the avoidance of using laparoscopy for diagnosing EP, medical and expectant treatments have become the focussed strategies. It is very important to select EP's subset which is conformable with treatment strategy to avoid risks to the patient [7]. Using the method of EM and methotrexate, Trio D et al. [8] and Dhar H et al. [2] received an 88% (β-hcg less than 1000 IU/l) and 65% complete resolution (success) rate respectively. For ruptured EP cases, either mini-laparotomy or laparoscopy is used in surgical therapy [9]. Between laparotomy and laparoscopy, the latter is considered mostly while the former is selected for patients with corneal EP or hemodynamic instability. Inexperienced surgeons and patients with difficult laparoscopic approach also prefer laparotomy [10]. According to many studies, laparoscopy of EP proves fewer cases of post-operative adhesions in comparison with laparotomy. Moreover, blood loss is lesser in laparoscopy so there is a reduced need for analgesia [10, 11]. The purpose of the study is to find the success rate of treating the unruptured TEP having 1 to 3 thousand IU/L β-hcg either with EM or methotrexate. At the same time, to find whether EM or medical treatment is better while dealing with the unruptured TEP having 1 to 3 thousand IU/L β-hcg as the local data on this topic is scarcely available, especially in this locality.

### Operational Definitions

- **TEP:** A fallopian tubes pregnancy diagnosed through ultra-sonography with a echogenic, thick circular structure present outside the uterus, having a gestational sac (echogenic ring with thickness that surrounds sonolucent centre conforming to the reaction of trophoblastic decidua around the chronic sac) with no cardiac activity and lastly, having 1 to 3 thousand IU/L β-hcg.
- **Medical Management:** Giving patients one methotrexate intra-muscular injection with 50 mg/m2 dose.
- **EM:** We monitored the patients for a week considering measurements of serial β-hcg and ultra-sonography as per local protocol demands.
- **Outcome:** We recorded reduced β-hcg levels and absence of gestational sac, pelvic-free fluid and adnexal mass (complete resolution) on ultra-sonography as successful. If the levels of β-hcg are more than 3000 IU/L with incomplete resolution, we recorded the outcome as unsuccessful.

## MATERIAL AND METHODS:

**Study Design:** A Randomized-controlled trial.

**Setting: This study was conducted at eh** Dept. of Obstetrics & Gynaecology at Mayo Hospital Lahore in the duration from October 2017 to April 2018.

**Inclusion Criteria:**

- Patients with TEP (according to operational definition) with 1 to 3 thousand IU/L β-hcg levels.
- Less than 4cm of ectopic mass.
- Having 18 to 40 years' age.

**Exclusion Criteria:**

- Patients with non-tubal EP.
- Patients with β-hcg levels less than/more than 1000 and 3000 IU/L respectively.
- More than 4cm ectopic mass.
- Patients having ruptured EP.
- Patients unstable hemodynamically.
- Fetal cardiac activity is present.
- Renal/hepatic failure.
- Heterotopic pregnancy.
- Hypersensitivity to methotrexate.
- Patients unwilling to inclusion.

We took eighty-two pregnant women, fulfilling inclusion criteria, with the permission of Local Ethical Committee. We informed all patients of the purpose, procedure, potential hazards and anticipated benefits before the study. An experienced gynaecologist (having 05 years' post-fellowship experience) was available for further details if required for both researcher and patients. We took informed consent and divided patients into group A and B through lottery method. Group A was treated through EM while Group B with methotrexate dose of 50 mg/m2 (medical management). After one week, we measured the outcome. We considered successful outcome with less than 10 β-hcg levels (negligible)

and complete resolution but unsuccessful if β-hcg levels were more than 3000 IU/L and incomplete resolution.

We analysed data through SPSS v.20.0 taking β-hcg levels and GA as mean ± SD and presenting results as percentage and frequency. We used Chi-square to compare successful/unsuccessful results of both groups. Statistically significant value of P was ≤0.05. We used matched-stratification tables for GA, patients' age, and β-hcg levels to control confounding variables.

**RESULTS:**

The study took 18-40 years' patients having 30.5±6.5 years as mean age. The mean age in group A and B was 30.9±5.9 and 30.6±6.3 years respectively. We found 57.3% (47) patients between 31-40 years' age. Mean GA was 7.4±2.2 weeks. Mean GA in group A and B was 7.1±2.1 and 7.6±2.4 weeks respectively. Most of the patients (51.2% or 42) had GA > six weeks. The mean levels of β-hcg in group A and B were 1584.6±515.8 and 1537.3±519.6 IU/L respectively. We found 90.2% (37) and 63.41% (26) patients with successful outcome (complete resolution and negligible β-hcg levels) among group A (EM) and group B (MM) respectively with p-value 0.004 within one week.

**Table – I:** Group-Wise Success Rate

| Outcomes | Group - A (41) | | Group - B (41) | |
|---|---|---|---|---|
| | No | % | No | % |
| **Successful** | 37 | 90.200 | 26 | 63.410 |
| **Unsuccessful** | 4 | 9.700 | 15 | 36.500 |

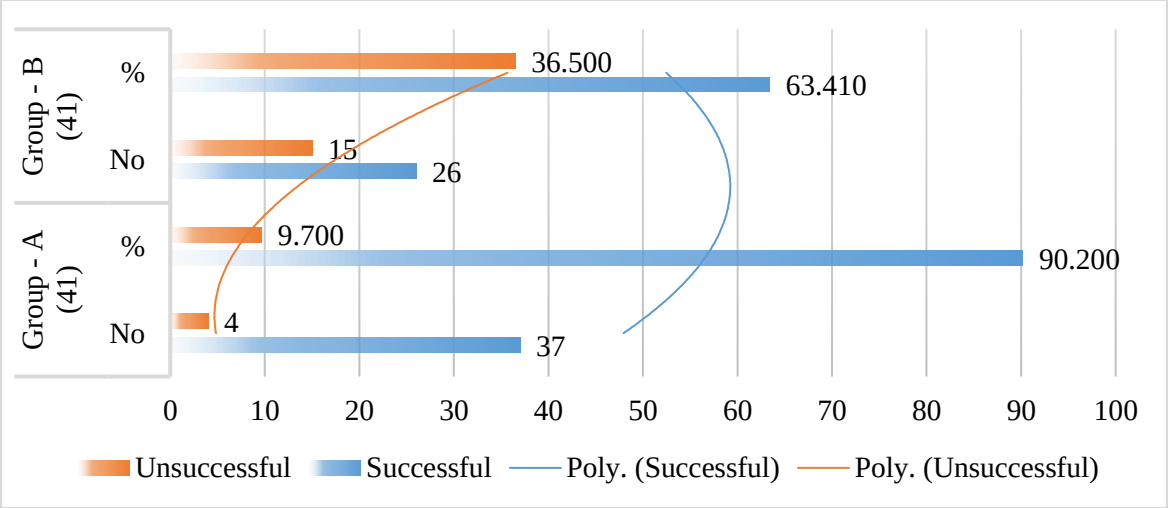



**Table – II:** Age, GA and B-hcg Distribution

| Details | | Group - A (41) | | Group - B (41) | | Total (82) | |
|---|---|---|---|---|---|---|---|
| | | No | % | No | % | No | % |
| Age (Years) | 18 - 30 | 18 | 43.90 | 17 | 41.46 | 35 | 42.60 |
| | 31 - 40 | 23 | 56.10 | 24 | 58.54 | 47 | 57.30 |
| GA (Weeks) | ≤ 6 | 19 | 46.30 | 21 | 51.20 | 40 | 48.70 |
| | > 6 | 22 | 53.60 | 20 | 48.70 | 42 | 51.20 |
| Level of B-hcg | 1000 - 2000 | 33 | 80.40 | 32 | 78.05 | 64 | 79.20 |
| | > 2000 - 3000 | 8 | 19.50 | 9 | 21.90 | 17 | 2.70 |

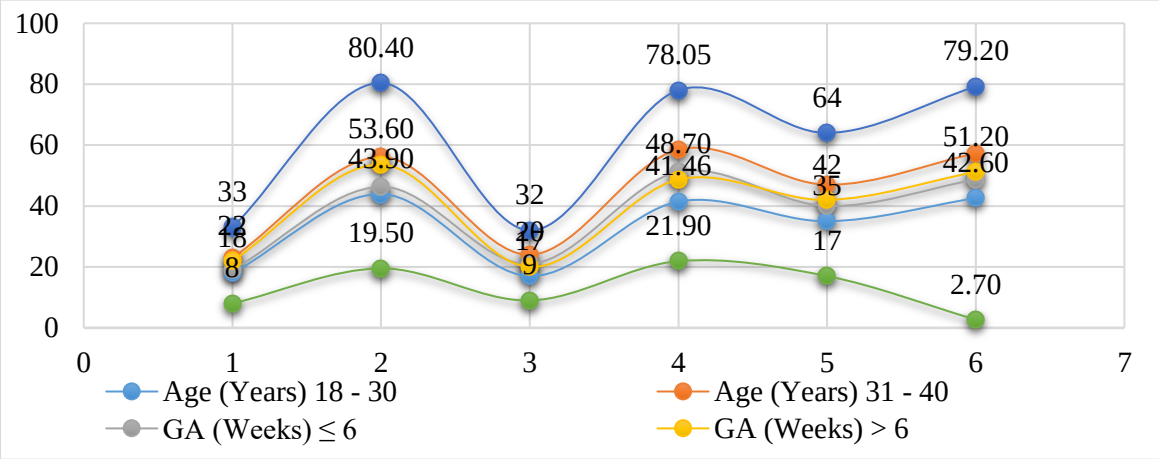
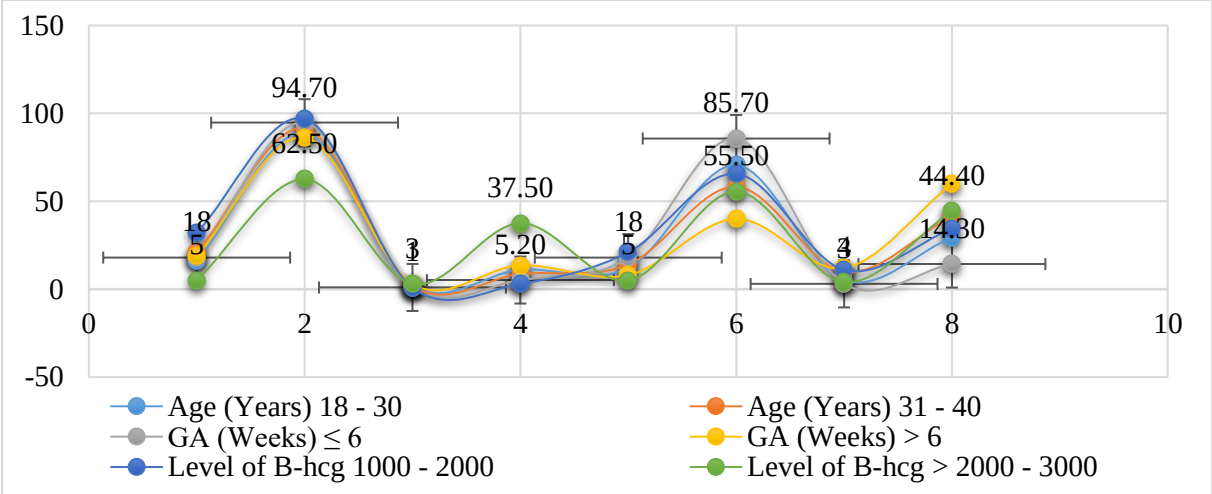



**Table – III:** Age, GA and B-hcg (Mean ± SD) Distribution

| Details | Group - A (41) | | Group - B (41) | | Total (82) | |
|---|---|---|---|---|---|---|
| | Mean | ± SD | Mean | ± SD | Mean | ± SD |
| Age | 30.9010 | 5.9500 | 30.5000 | 6.5000 | 30.6000 | 6.3000 |
| GA | 7.1000 | 2.1000 | 7.6000 | 2.4000 | 7.4000 | 2.2000 |
| Level of B-hcg | 1584.6000 | 151.8000 | 1537.3000 | 519.6000 | 1565.4000 | 517.8000 |

**Table – IV:** Age, GA and B-hcg Success Rate Distribution

| Outcomes | | | Age (Years) | | GA (Weeks) | | Level of B-hcg | |
|---|---|---|---|---|---|---|---|---|
| | | | 18 - 30 | 31 - 40 | ≤ 6 | > 6 | 1000 - 2000 | > 2000 - 3000 |
| Group - A (41) | Successful | No | 16 | 21 | 18 | 19 | 32 | 5 |
| | | % | 88.80 | 91.30 | 94.70 | 86.30 | 96.90 | 62.50 |
| | Unsuccessful | No | 2 | 2 | 1 | 3 | 1 | 3 |
| | | % | 11.10 | 8.70 | 5.20 | 13.60 | 3.03 | 37.50 |
| Group - B (41) | Successful | No | 12 | 14 | 18 | 8 | 21 | 5 |
| | | % | 70.50 | 58.30 | 85.70 | 40.01 | 65.60 | 55.50 |
| | Unsuccessful | No | 5 | 10 | 3 | 12 | 11 | 4 |
| | | % | 29.40 | 41.60 | 14.30 | 60.01 | 34.30 | 44.40 |
| P Value | | | 0.17 | 0.1 | 342 | 0.002 | 0.001 | 0.772 |




**DISCUSSION:**

The improved early diagnose has increased EP incidence. EP lead to tubal abortion or complete re-absorption because it did not diagnose in time clinically. Some researchers prefer EM in the early diagnosis, however, separating proliferative EP from ETPs can be a clinical problem [12]. Lund (1955) was the 1st to practice EM among EP suspected patients who were un-distressed of admission [11]. As treatment of Eps through natural course resulted in re-absorption or tubal abortion, researchers suggested EM. Since EM is advocated, a less number of studies have been published giving details of patients with EP, no cardiac activity, higher hCG serum concentration that reduced (progesterone concentration low) [12]. Serum hCG must be monitored closely to detect an inadequate reduction of hCG concentration. There are no clear criteria for therapeutic intervention. A study described the dynamics of serum-hCG during a spontaneous resolution of EP [13].

Women with EP visible, plateauing/low serum-hCG concentrations are however treated with methotrexate [14]. The early Eps may follow a self-limiting process of natural course, leading to re-absorption/tubal abortion. Many studies suggested watchful waiting as a safe alternative treating EPs [15] but there is less evidence of these studies. Our study compares EM with MM among patients with unruptured TEP with β-hcg 1-3 thousand IU/L. We found 90.2% (37) and 63.41% (26) patients with successful outcome (complete resolution and negligible β-hcg levels) among group A (EM) and group B (MM) respectively with p-value 0.004 within one week. Trio D et al. [8] and Dhar H et al. [2] found a success rate of 88% and 65% among patients with EP having β-hcg less than 1000 IU/L, through EM and methotrexate respectively. β-hcg levels predict the success of medical treatment. Lipscomb et al. found more than 90% success using a single dose of methotrexate having β-hcg level <5000 mIU/mL which reduced to 80% and 70% when levels increased from 5-10 and then 15 thousand mIU/mL respectively [13]. Srivichai et al. found a 90% success rate among 96/106 patients through methotrexate with giving a 2nd dose to 4 patients [16]. Merisio's series found a 90% (10/11 patients) success rate with single-dose treatment [17].

The published literature shows a 67-100% range of success through single Vs. multi-dose treatment of EPs [18]. Mahboob recorded 80% success rate among 12/15 patients with single-dose methotrexate having levels of β-hcg=5000mIU/mL [19]. The study searched for EM of EP relevant data published between 1992-2004 through Medline search where we found 48-100% success rates [20, 21]. The success rate was 65.30% (77 out of 118 patients) in the largest study to this date [81]. Our study assessed 81 every 1-3 days using serum-hCG and TVS until the levels of hCG were <10 IU/L. Time of resolution was 4-67 (mean=20) days. The levels of hCG were much lower initially with successful EM compared to failed EM (374 Vs. 741 IU/L). For spontaneous resolution, the success rate was 88% with hCG level <200 IU/L while 25% at the >2000 IU/L levels. Similar results show a 96% success with hCG levels <175 IU/L [12]. We found a single RCT (Randomised Controlled Trail) with the comparison of EM to systematic methotrexate. This study included sixty hemodynamically stable women treated with 2.50mg/day of placebo or oral methotrexate for five days [22]. We used determination of serum-hCG and TVS to diagnose EPs. We found no significant difference between the

two methods with 77% of success rate overall. However, the treatment used methotrexate with low dose so the median baseline hCG levels were low [22].

## CONCLUSION:

The study concludes EM to have better outcomes with negligible levels of β-hcg and complete resolution comparing MM among women with TEP having β-hcg between 1-3 thousand IU/L. Hence, we recommend EM over medical management to reduce/avoid tubal injury with better fertility outcomes.

## REFERENCES:


1. Verma U, English D, Brookfield K. Conservative management of nontubal ectopic pregnancies. Fertil Steril. 2011;96(6):1391-95.
2. Helmey S, Sawyer E, Ofili-Yebovi D, Yazbek J, Nagi JB, Jurkovic J. Fertility outcomes following expectant management of tubal ectopic pregnancy. Ultrasound Obstet Gynecol. 2007; 30:988–93.
3. This EW, Loi K, Wang JJ, Siow A. Methotrexate treatment for ectopic pregnancy at the KK Women's and Children's Hospital, Singapore. Singapore Med J. 2009;50(11):1058-61.
4. Van Mello NM, Mol F, Opmeer BC, Ankum WM, Barnhart K, Coomarasamy A, et al. Diagnostic value of serum hCG on the outcome of pregnancy of unknown location: a systematic review and meta-analysis. Hum Reprod Update. 2012;18(6):603–17.
5. Van Mello NM, Mol F, Verhoeve HR, van Wely M, Adriaanse AH, Boss EA, et al. Methotrexate or expectant management in women with an ectopic pregnancy or pregnancy of unknown location and low serum hCG concentrations? a randomized comparison. Hum Reprod. 2012; 10:1-8.
6. Dhar H, Hamdi I, Rathi B. Methotrexate Treatment of Ectopic Pregnancy: experience at Nizwa Hospital with Literature Review. Oman Med J. 2011;26(2):94-8.
7. Jurkovic D. Ectopic pregnancy. In: Edmonds DE. Dewhurst's Textbook of obstetrics and gynaecology. (8thed.) UK: Wiley-Blackwell; 2012:76-87.
8. Trio D, Strobelt N, Picciolo C, Lapinski RH, Ghidini A. Prognostic factors for successful expectant management of ectopic pregnancy. Fertil Steril. 1995;63(3):469-72.
9. Crochet JR, Bastian LA, Chireau MV. Does this woman have an ectopic pregnancy? the rational clinical examination systematic review. JAMA. 2013;309(16):1722–9.
10. Skipworth R. A new clinical sign in ruptured ectopic pregnancy. Lancet. 2011;378(9809): e27.
11. Mol F, van den Boogaard E, van Mello NM, van der Veen F, Mol BW, Ankum WM, et al. Guideline adherence in ectopic pregnancy management. Hum Reprod. 2011;26(2):307-15.
12. Elson J, Tailor A, Banerjee S, Salim R, Hillaby K, Jurkovic D. Expectant management of tubal ectopic pregnancy: prediction of successful outcome using decision tree analysis. Ultrasound Obstet Gynecol. 2004; 23:552–6.
13. Korhonen J, Stenman UH, Ylöstalo P. Serum human chorionic gonadotropin dynamics during spontaneous resolution of ectopic pregnancy. Fertil Steril. 1994; 61:632–6.
14. Hajenius PJ, Mol F, Mol BW, Bossuyt PM, Ankum WM, van der Veen F. Interventions for tubal ectopic pregnancy. Cochrane Database Syst Rev. 2007:CD000324.
15. Kirk E, Van Calster B, Condous G, Papageorghiou AT, Gevaert O, Van Huffel S, et al. Ectopic pregnancy: using the hCG ratio to select women for expectant or medical management. Acta Obstet Gynecol Scand. 2011; 90:264–272.
16. Srivichai K, Uttavichai C, Tongsong T. Medical treatment of ectopic pregnancy: a tenyear review of 106 cases at MaharajNakorn Chiang Mai Hospital. J Med Assoc Thai. 2006 Oct;89(10):1567-1571.
17. Merisio C, Anfuso S, Berretta R, Gualdi M, Pultrone D et al . Single –dose methotrexate for Ectopic pregnancy treatment: preliminary data Acta Bio Med. 2005;76: 33-36.
18. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. ObstetGynecol 2003 Apr;101(4):778-784.
19. Mahboob U, Mazhar SB. Management of ectopic pregnancy: a two-year study. J Ayub Med Coll Abbottabad 2006 Oct-Dec;18(4):34-37.
20. Ylostalo P, Cacciatore B, Sjoberg J, Kaariainen M, Tenhunen A, Stenman UH. Expectant management of ectopic pregnancy. ObstetGynecol1992; 80: 345–348.
21. Korhonen J, Stenman UH, Ylostalo P. Serum human chorionic gonadotropin dynamics during spontaneous resolution of ectopic pregnancy. FertilSteril1994; 61:632–636.
22. Korhonen J, Stenman UH, Ylostalo P. Lowdose oral methotrexate with expectantmanagement of ectopic pregnancy. Obstet Gynecol. 1996; 88:775–778.