

## Treatments and Outcomes of Patients Diagnosed With Tubal Pregnancy at Wichian Buri Hospital

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**Background:** Treatment options of tubal pregnancy include medical and surgical treatments and the outcomes is associated with an appropriate patient selection. However, the limitation of hospital resource may influence the treatment options and also outcome.

**Objective:** To evaluate patients diagnosed with tubal pregnancy including treatment method and outcomes of treatment at Wichian Buri Hospital.

**Methods:** Fifty-five women diagnosed with ectopic pregnancy who were treated at Wichian Buri Hospital, from January 2017 to December 2020 were included in the retrospective study. The clinical data was recorded. The treatment option and outcomes were collected.

**Results:** The mean maternal age was 29 years (SD, 7.3 years). Most of the cases had no known risk factor such as the history of sexually-transmitted infection and no previous pelvic surgery. There were 38 patients (69.1%) presented with more than 1 symptom including pain and bleeding and the total of 48 patients (87.3%) reported symptom of pain. Most of the cases (63.6%) were diagnosed with unruptured ectopic pregnancy. Comparing ruptured and unruptured ectopic pregnancies, there was no statistical difference in clinical data except for the size of the adnexal mass, which was smaller in the ruptured group ( $P = .01$ ). All ruptured tubal pregnancy underwent surgery which was salpingectomy. The majority of unruptured ectopic pregnancies also underwent surgical treatment (65.7%).

**Conclusions:** The treatment of ectopic pregnancy in Wichian Buri Hospital was comparable to the standard treatment. The surgical management was the majority of treatment options that were selected regarding to the limitation. However, the outcomes were acceptable.

**Keywords:** Tubal pregnancy, Outcomes, Treatment

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## Introduction

Tubal pregnancy occurs in approximately 1% to 2% of pregnancies.<sup>1</sup> The incidence seems to be increasing and sometimes can be life-threatening under certain conditions. Ectopic pregnancy could be a cause of significant morbidity and mortality, as well as future fertility.<sup>2</sup> However, early diagnosis could lessen the risk of a deleterious outcome. Ectopic pregnancy can be associated with various risk factors including previous history of extrauterine pregnancy, abnormal fallopian tubes, pelvic inflammatory disease, endometriosis, and previous pelvic organ surgery.<sup>2</sup>

Treatment options for ectopic pregnancy include surgical and nonsurgical treatment. Systemic methotrexate (MTX) was revealed as an effective treatment in a well-selected unruptured ectopic pregnancy.<sup>3</sup> Nevertheless, the selection of treatment is regarded as presenting symptoms, availability of medication and feasibility of treatment which is dependent on the capability of the hospital.

Different levels of the hospital may be affected by the capacity to provide treatment differently. For example, lacking laboratory testing of serum  $\beta$  human chorionic gonadotropin ( $\beta$ -hCG) would affect the decision-making of the doctor not to choose the conservative option. A common nonsurgical treatment is methotrexate administration, which delivers favorable outcomes in well-selected cases.<sup>2</sup> Nevertheless, treatment would also be dependent on the doctor's preference and skills as well as the ability to follow-up with patients.

Wichian Buri Hospital is classified as a middle-level medical facility (M1 categorized by the Ministry of Public Health, Thailand) with the capacity to admit patients for almost 241 beds and is responsible for 3 adjacent districts. Many different forms of ectopic pregnancy have presented at the hospital and various treatments were provided according to the patients' clinical presentations, the feasibility of medication, and the operating theater available at the time. However, there was no definite local guideline for treatment.

This study aimed to evaluate patients diagnosed at the hospital and the outcomes of treatment compared to previous reports. As a result, an appropriate local guideline could be developed to deliver the best treatment option for patients in a limited resource setting.

## Methods

This retrospective study was conducted on 55 women diagnosed with ectopic pregnancy who were treated at Wichian Buri Hospital, Phetchabun, Thailand from January 2017 to December 2020. Even this descriptive study aimed to evaluate the treatment in 1 institute, the sample size calculation estimated 48 cases at an  $\alpha$  level of .10, population proportion of 0.77 referenced from Olofsson et al,<sup>3</sup> and error of 10%. The additional 10% drop-off sample was calculated, the total number of samples were 52 cases.

### Ethics

This study was approved by the Ethical Review Committee for Human Research, Phetchabun Provincial Public Health Office (2/65-26-7/04/65 on April 7, 2022).

### Study Design

Data were obtained from electronic hospital records including medical records, treatment records, operative notes, and discharge summaries. The demographic data, clinical presentation, initial and subsequent  $\beta$ -hCG levels, as well as outcomes of treatment, were collected. All patients had at least a value of  $\beta$ -hCG record.

### Statistical Analysis

Data were analyzed and presented in descriptive statistics as mean, range, and standard deviation (SD). In comparison, statistics, chi-square test, Fisher exact test, student  $t$  test, and Mann-Whitney  $U$  test were applied. A  $P$  value less than .05 was considered statistically significant. Statistical analysis was carried out using STATA version 16 (StataCorp. Version 16. College Station, TX: StataCorp LLC; 2019).

## Results

This study included 55 cases of ectopic pregnancy with complete medical data (mean [SD] age, 29 [7.3]; range, 16 - 50 years). The mean (SD) body mass index was 23.0 (4.6) kg/m<sup>2</sup>. The majority of patients had a previous pregnancy (38.2%) and had no previous abortions (70.9%). Most patients did not use any contraception (78.2%) and did not smoke. According to the risk factors, most of the cases had no history of sexually-transmitted infection and no previous pelvic surgery. Fifty-five patients reported symptoms when diagnosed ectopic pregnancy. There were 38 patients (69.1%) presented with more than 1 symptom including pain and bleeding and the total of 48 patients (87.3%) reported symptom of pain. There were 46 patients had the record of the size of adnexal mass (median [range], 2.9 [0 - 8] cm), and the majority of cases had no yolk sac or fetal echo identified. There were no record of serum  $\beta$ -hCG in 7 patients which presented with ruptured ectopic pregnancy. Those 7 patients underwent emergency surgical treatment and confirmed ruptured. Among those who had the record of serum  $\beta$ -hCG, pretreatment serum  $\beta$ -hCG was 3844.2 IU/L, and 7 cases had no record of serum  $\beta$ -hCG level. Most of the cases were diagnosed with unruptured ectopic pregnancy (63.6%) (Table 1).

Comparing ruptured and unruptured ectopic pregnancies, there was no statistical difference in clinical data except for the size of the adnexal mass, which was smaller in the ruptured group, 1 cm in ruptured group and 3.2 cm in unruptured group ( $P = .01$ ). Among 80% of patients in the unruptured group had no yolk sac or fetal echo compared to more than 50% in the ruptured group, who presented with a positive yolk sac or fetal echo on ultrasonography. The majority of unruptured ectopic pregnancies also underwent surgical treatment (65.7%). Characteristics of patients among treatment modalities, including observation, methotrexate, and surgery, were analyzed and there was no statistical difference among groups. All of 18 patients who presented with ruptured tubal pregnancy were undergone emergency surgical treatment with salpingectomy. Most of unruptured

**Table 1. Demographic Data**

Variable	No. (%)
Age, mean (SD), y	29.0 (7.3)
Parity	
0	17 (30.9)
1	21 (38.2)
2	9 (16.4)
3	2 (3.6)
Missing data	6 (10.9)
Previous abortion	
No	39 (70.9)
Yes	10 (18.2)
Missing data	6 (10.9)
Contraceptive methods	
None	43 (78.2)
Combined pills	3 (5.4)
Postcoital pills	5 (9.1)
TR	1 (1.8)
Missing data	3 (5.4)
Smoking	
No	55 (100)
History of STD infection	
No	53 (96.4)
Yes	2 (3.6)
Gestational age, mean (SD), wk	8.3 (2.8)
Presenting symptoms	
None	2 (3.6)
Pain	10 (18.2)
Bleeding	5 (9.1)
Pain and bleeding	38 (69.1)
Diameter of adnexal mass (n = 46), median (min - max), cm	2.9 (0 - 8)
Presence of yolk sac or fetal echo	
No	38 (69.1)
Yes	17 (30.9)
Pretreatment $\beta$ -hCG level, median (min - max), IU/L	3844.2 (418.1 - 206 932.0)



**Table 1. Demographic Data (Continued)**

Variable	No. (%)
Treatment modalities	
Observe	6 (10.9)
Methotrexate	8 (14.5)
Surgery	41 (74.6)
Rupture	
No	35 (63.6)
Yes	18 (32.7)
Loss follow-up	2 (3.7)

Abbreviations:  $\beta$ -hCG,  $\beta$  human chorionic gonadotropin; SD, standard deviation; STD, sexually transmitted disease; TR, tubal resection.

tubal pregnancy patients also underwent surgical management with salpingectomy. Neither salpingostomy nor salpingotomy were reported.

A total of 8 cases underwent methotrexate administration with 6 confirmed successes without any other treatment. There were 2 patients who were lost to follow-up. The clinical data of 8 patients received methotrexate treatment which was a small number in this hospital. The initial serum  $\beta$ -hCG level ranged from 418.14 IU/mL to 8910.04 IU/mL (Table 2). However, the size of the adnexal mass was not correlated with the  $\beta$ -hCG level.

Among those diagnosed with an ectopic pregnancy in this period, 19 cases presented with clinically-considered ruptured ectopic pregnancy and underwent surgery.

**Table 2. Characteristics of Patients Receiving Methotrexate**

Case No.	Age, y	Gestational age, wk	Adnexal mass, cm	$\beta$ -hCG Level, IU/L		
				Day 1	Day 4	Day 7
19	18	NA	2.3	718.26	603.76	338.69
20	50	NA	2.7	8910.04	3003.62	1921.53
37	28	8	8.0	1018.71	825.05	261.31
39	24	NA	1.7	418.14	51.83	18.57
41	27	NA	3.5	1449.00	783.50	462.97
42	19	8	2.0	1852.00	NA	NA
47	28	7	4.0	7646.39	7256.42	2619.83
54	33	9	0	2010.98	NA	NA

Abbreviations:  $\beta$ -hCG,  $\beta$  human chorionic gonadotropin; NA, not available.

## Discussion

Ectopic pregnancy is not uncommon and is associated with various risk factors (age, previous ectopic pregnancy, contraception, and underlying diseases). A significant factor is previous pelvic surgery. The common presenting symptoms are pelvic pain, missed periods, and abnormal vaginal bleeding.<sup>2</sup> In the present study, most of patients had no significant risk factors and presented with more than 1 symptom including abnormal vaginal bleeding and pelvic pain. Every patient reported a missed period.

This could be from the small number of patients enrolled. As a result, the significant factors related to ectopic pregnancy in these groups could not be concluded.

Avcioğlu et al<sup>1</sup> reported that size and initial serum  $\beta$ -hCG are associated with the outcome of medical treatment. Serum  $\beta$ -hCG level of less than 1000 IU/L provided 86.3% success rate for methotrexate treatment, while the success rate decreased to 42.3% on  $\beta$ -hCG levels of more than 3000 IU/L. In the present study, the highest initial serum  $\beta$ -hCG was 8910.04 IU/L with a 2.7 cm adnexal mass, and this patient had success with medical treatment.



Nevertheless, only 1 patient encountered this condition. To determine the factors associated with treatment outcomes, a greater number of patients may be needed. The American College of Obstetricians and Gynecologists<sup>4</sup> proposed that well-selected patients for medical treatment would result in favorable outcomes. The choice of treatment should be considered regarding patient condition, preference and feasibility. These could be changed depending on the capability of the medical institute. However, methotrexate may not be available at Wichian Buri Hospital, thus influencing the selection of treatment. This would also affect treatment at our hospital as the majority of patients undergo surgical treatment.

The size of the adnexal mass seemed to be larger in the unruptured group, with a mean (range) diameter of 1 (0 - 8) cm in the ruptured and 3.2 cm in the unruptured group ( $P = .01$ ). The rationale of this finding, which was different from other research, could be due to the well-defined border of the adnexal mass in the unruptured group. On the contrary, the adnexal mass in the ruptured group would be included in blood clots and usually revealed as a complex mass, so it might be difficult to identify the actual size.

Systemic intramuscular methotrexate administration of 50 mg/m<sup>2</sup> is a safe and effective treatment option for unruptured and well-selected ectopic pregnancies. The success rate was reported to be almost 80% with the mean (SD) time to resolution of 24 (9) days.<sup>3</sup> The outcome of medical treatment in our study was comparable to the literature. However, the small number of cases would affect the strength of this result. Ranchal et al<sup>5</sup> assessed that either exploratory or laparoscopic procedures provided comparable outcomes. Previous study in Chiang Mai, Thailand reviewed medical treatment for tubal pregnancy and found that the success rate was 96% in well-selected patient.<sup>6</sup> This result was comparable to other research and

would be a strong evidence to propose this option to be available in our hospital. There are 3 surgical procedures that would be applied to tubal pregnancy which are salpingostomy, salpingotomy, and salpingectomy. Salpingectomy was traditionally a standard surgical technique while the other 2 methods are conservative.<sup>7</sup> Nevertheless, those conservative technique do need surgical skills. In the contrary, the randomized controlled trials reported the comparable fertility outcome of salpingostomy and salpingectomy.<sup>8-10</sup> As a result of that, because our patient may be limit compliance to follow-up after surgery, salpingectomy might be appropriate. The option of any surgical procedure relies on many factors including shared decision making with patients. Despite laparoscopic surgery seemed to be the standard technique,<sup>7</sup> Wichian Buri Hospital has no laparoscopy, which requires special equipment in addition to significant resources and expenses. At our hospital, exploratory laparotomy is the first choice for surgical treatment and every case underwent salpingectomy. However, the recently up-level of the hospital would be associated with referred patients so various options should be adopted.

## Conclusions

The treatment of ectopic pregnancy in Wichian Buri Hospital was comparable to the standard treatment, but might not be available all the time. The outcome of surgical treatment was acceptable. As a result of the effectiveness of medical treatment, accessibility to methotrexate should be considered in the future. The early detection of ectopic pregnancy is a key hallmark for decreasing morbidity and mortality among patients diagnosed with ectopic pregnancy. An effective guideline for an ambulatory physician would provide patients with the ability to be treated as early as possible.

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## แนวทางและผลลัพธ์ของการรักษาผู้ป่วยที่ได้รับการวินิจฉัยตั้งครรภ์นอกรحمคู่กับ ที่โรงพยาบาลวิเชียรบุรี

พิรัณย์รัตน์ สงวนแห่ง

กลุ่มงานสุตินรีเวชกรรม โรงพยาบาลวิเชียรบุรี เพชรบูรณ์ ประเทศไทย

**บทนำ:** การรักษาการตั้งครรภ์นอกรحمคู่กับมีทั้งการรักษาด้วยการใช้ยาและการผ่าตัด ซึ่งผลการรักษาขึ้นอยู่กับการคัดเลือกผู้ป่วยที่เหมาะสม อย่างไรก็ตาม ข้อจำกัดของทรัพยากรของโรงพยาบาลมีผลต่อการเลือกวิธีการรักษาและผลของการรักษา

**วัตถุประสงค์:** เพื่อศึกษาผู้ป่วยที่ได้รับการวินิจฉัยว่ามีการตั้งครรภ์นอกรحمคู่กับที่โรงพยาบาลวิเชียรบุรี ทั้งแนวทางการรักษาและผลของการรักษา

**วิธีการศึกษา:** การศึกษาแบบย้อนหลังในกลุ่มตัวอย่างผู้ป่วยจำนวน 55 คน ที่ได้รับการวินิจฉัยว่ามีการตั้งครรภ์นอกรحمคู่กับที่โรงพยาบาลวิเชียรบุรี ระหว่างเดือนมกราคม พ.ศ. 2560 ถึงเดือนธันวาคม พ.ศ. 2563 โดยเก็บข้อมูลพื้นฐานทางคลินิก วิธีการรักษาที่ได้รับ และผลการรักษา

**ผลการศึกษา:** กลุ่มตัวอย่างผู้ป่วยมีอายุเฉลี่ยเท่ากับ 29 ปี (SD, 7.3) ส่วนใหญ่ของผู้ป่วยไม่มีประวัติที่มีปัจจัยเสี่ยง ได้แก่ ประวัติการมีโรคติดต่อทางเพศสัมพันธ์ และประวัติการได้รับการผ่าตัดในอุ้งเชิงกรานมาก่อน ผู้ป่วย จำนวน 38 คน มีอาการมากกว่า 1 อย่าง ได้แก่ อาการปวดและมีเลือดออกทางช่องคลอด ผู้ป่วยได้รับการวินิจฉัยว่าเป็นการตั้งครรภ์นอกรحمคู่กับที่ยังไม่แตกถึงร้อยละ 63.3 เมื่อเปรียบเทียบกลุ่มที่มีค่าใช้การตั้งครรภ์นอกรحمคู่กับที่แตกและไม่แตก พบว่า ไม่มีความแตกต่างกันทางสถิติของข้อมูลทางคลินิก ยกเว้นขนาดของการตั้งครรภ์ นอกرحمคู่กับที่มีขนาดเล็กกว่าในกลุ่มที่ได้รับการวินิจฉัยว่าตั้งครรภ์นอกรحمคู่กับที่แตก ( $P = .01$ ) ผู้ป่วยที่ได้รับการวินิจฉัยว่ามีการตั้งครรภ์นอกรحمคู่กับที่แตก ทั้งหมดได้รับการผ่าตัด โดยการตัดท่อนำไข่ออก และร้อยละ 65.7 ของผู้ป่วยที่ได้รับการวินิจฉัยว่าตั้งครรภ์นอกรحمคู่กับที่ได้รับการรักษาโดยการผ่าตัด

**สรุป:** แนวทางการรักษาการตั้งครรภ์นอกรحمคู่กับที่โรงพยาบาลวิเชียรบุรีเป็นไปตามการรักษามาตรฐาน การรักษาโดยการผ่าตัดเป็นการรักษาหลักที่ได้รับการเลือกเนื่องจากข้อจำกัดของโรงพยาบาล อย่างไรก็ตาม ผลการรักษานั้นเป็นที่ยอมรับได้

**คำสำคัญ:** การตั้งครรภ์นอกรحمคู่กับ การรักษา ผลการรักษา

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