

Evaluation of Spontaneous Fertility after Medical Treatment of Tubal Ectopic Pregnancy in Two Hospitals in the City of Yaounde

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Abstract

Background: Ectopic pregnancy is a major cause of maternal morbidity and mortality, estimated to occur in 1% - 2% of pregnancies worldwide. This condition also has an adverse effect on the fertility prospects of women who experience it. **Objective:** To determine the outcomes of subsequent spontaneous fertility after medical treatment of patients with methotrexate (MTX) in patients with ectopic pregnancy at two university teaching hospitals of Yaounde. **Methodology:** We carried out a cross-sectional study with retrospective data collection in two university teaching hospitals of Yaounde during a six years period from 1st January 2015 to 31st May 2021. Seventy records of patients who had medical treatment for ectopic pregnancy were included in this study. Statistical analysis was performed using SPSS. 23. The Chi-2 statistical test was used to compare qualitative variables. Binary logistic regression method was performed to identify independent risk factors associated with infertility after medical treatment of tubal ectopic pregnancy (TEP). The significance level was set at 0.05. **Results:** The mean age in our study population was 27.8 ± 3.8 years. According to the past medical history, 52.9% had a pelvic inflammatory disease (PID) and the most frequently germ found was *C. trachomatis* (47.1%). Almost 15% of our study population had previous surgery for EP. The median Fernandez score was 11 with a minimum score of 4 and a maximum score of 13. The route of administration of methotrexate was intramuscular in all our patients, and the single-dose protocol was used most frequently (58.6%). After medical treatment of the EP, we found a spontaneous conception rate of 58.6%. After multivariate analysis, we were unable to confirm that there was an association between a history of sexually transmitted infections (STIs) and fertility prognosis. **Conclusion:** The spontaneous fertility rate after medical management of EP was 58.6%, of which 73.2% were

term pregnancies and 14.6% were recurrent ectopic pregnancies.

Keywords

Ectopic Pregnancy, Maternal Morbidity

1. Introduction

Ectopic pregnancy, an important cause of maternal morbidity and mortality, is estimated to occur in approximately 1% - 2% of pregnancies worldwide [1]. Tubal localization accounts for 95% - 99% of ectopic pregnancies. Other localizations such as ovarian, cervical, cornual, and abdominal implants are rarely seen [2]. Chlamydia trachomatis infection of the genital tract, the most common sexually transmitted infection with a worldwide distribution, plays a key role in the occurrence of this localization [3]. Indeed, tubal infection by *C. trachomatis*, damages ciliated epithelium leading to the formation of intraluminal adhesions that predispose to entrapment of the zygote and the resultant ectopic implantation of the blastocyst.

Over the last 20 years, considerable progress has been made in the management of ectopic pregnancy. Conservative laparoscopic surgery is currently the cornerstone of treatment for tubal pregnancies in women who desire future fertility, while treatment with systemic methotrexate may, however, offer better prospects for fertility by avoiding surgical trauma to the tube. So what about reproductive outcomes for patients with EP? Clarifying the impact of each treatment modality on natural pregnancy outcomes to help tubal EP patients with fertility needs choose appropriate treatment. Hao *et al.* found that there was a significant difference in the chances of subsequent intrauterine pregnancy in tubal EP patients treated with MTX compared with those treated with surgery [odds ratios (OR) = 1.52, 95% confidence interval (CI): 1.20 - 1.92] [4].

Several studies had evaluated fertility outcomes subsequent to medical and surgical treatment for ectopic pregnancy patients, with a cumulative incidence of intra uterine pregnancy up to 60% [2] [4], but none in our settings evaluates outcomes of fertility after medical treatment [5]. We therefore sought to determine the outcomes of subsequent spontaneous fertility after medical treatment of patients with MTX in patients with ectopic pregnancy at two university hospitals in the city of Yaounde.

2. Methodology

2.1. Type of Study

We conducted an analytical cross-sectional study with retrospective data collection.

2.2. Study Site

The study took place in maternity wards of university teaching hospitals in

Yaounde: the Yaounde Central Hospital (YCH), the Yaounde Gyneco-Obstetrics and Pediatrics Hospital (YGOPH).

2.3. Period/Duration of the Study

The study covered a period of 06 years five months, from 1st January 2015 to 31st May 2021. The duration of the study was seven months from 1st November 2023 to 1st May 2023.

2.4. Study Population

1) Target population

Records of patients who had medical treatment for ectopic pregnancy in the study sites during study period.

2) Source population

Records of women of childbearing age diagnosed and treated for EP in the study sites during study period.

3) Sampling

The sampling was consecutive and exhaustive. Seventy patients (70) were recruited during the study period.

a) Inclusion criteria

We included all records of women diagnosed and treated medically with success for tubal ectopic pregnancy, who had conceived or not within two years of treatment and who had given their consent for the study.

b) Non-inclusion criteria

Records of women diagnosed and treated medically with success for tubal ectopic pregnancy with contraception.

c) Exclusion criteria

Records of patients who had undergone assisted reproductive technologies (ART), and patients whose records could not be analyzed were excluded from our study.

2.5. Procedure and Ethical Considerations

After obtaining ethical approval and authorization for the research from the ethics committee of the Faculty of Medicine and Biomedical Sciences at the University of Yaoundé I and from hospital managers, patient records were selected from hospital registers. A pre-tested survey form was used to record sociodemographic and clinical characteristics and the treatment protocol used. By telephone interview, we presented the study to the patients, obtained their verbal consent and completed the missing information, in particular the notion of spontaneous conception or not, and the average time to conception after medical treatment.

2.6. Statistical Analysis

Data were entered and analyzed using CSPro7.1 and SPSS 23.0. Tables were

prepared using Microsoft Office Excel and Word 2013. The mean, standard deviation and median were calculated for quantitative variables, and the frequency, number of participants for qualitative variables. The Chi-2 statistical test was used to compare qualitative variables. The significance level was set at 5%, or 0.05.

3. Results

3.1. Sociodemographic Characteristics

Table 1 shows the distribution of patients according to socio-demographic data. In our study, the most common age range was [21 - 35] years (95.7%); 31 patients (44.3%) were single; 55.7% had a university education and 34.3% (24 patients) were still at school. The mean age in our study population was 27.8 ± 3.81 , with extremes ranging from 20 to 37 years.

3.2. Past Medical History

Table 2 shows the distribution according to history of EP. 37 patients (52.9%) had a pelvic inflammatory disease and the most frequent germ found was *Chlamydia trachomatis* (47.1%); 10% of patients had a history of tubal obstruction; 10 patients (14.3%) had already undergone surgery for EP.

3.3. Characteristics of EP

The median gestational age of EPs was 6 weeks' amenorrhea, with extremes ranging from 4 weeks' to 12 weeks' amenorrhea; the most affected tube was the

Table 1. Distribution of patients according to age, marital status and study level.

Variables	Size (N = 70)	Percentage (%)
Age (years)		
[16 - 20]	2	2.9
[21 - 35]	67	95.7
[36 - 40]	1	
[>40]	0	
Marital status		
Single	31	44.3
Cohabiting	13	18.6
Married	26	37.1
Niveau d'étude		
None	0	0
Primary	2	2.9
Secondary	29	41.4
Higher	39	55.7

Table 2. Distribution of patients according to risk factors for EP.

Variables	Size (N = 70)	Percentage (%)
History of tubal obstruction		
Yes	7	10.0
No	63	90.0
Gynecological congenital malformation		
Yes	0	0
No	70	100
History of STIs		
Yes	43	61.4
No	27	38.6
C. Trachomatis infection		
Yes	33	47.1
No	37	52.9
History of pelvic surgery		
Yes	10	14.3
No	60	85.7

right tube in 51.4% and the most affected tubal segment was the ampulla in 61.4%; the median Fernandez score was 11 with a minimum score of 4 and a maximum score of 13 (**Table 3**).

3.4. Medical Therapeutic Protocol

The administration route of methotrexate was intramuscular in all our patients, and the single-dose protocol was used most frequently (58.6%). The initial B-HCG level was <3000 IU in 75.7% of cases and at Day 7, this level was less than 1000 IU in 51.4% of cases; the percentage of BHCG reduction during the first week ranged from 40% to 70% (**Table 4**).

3.5. Spontaneous Conception after Medical Treatment of EP

After medical treatment of the EP we had a spontaneous conception rate of 58.6% (**Table 5**).

3.6. Factors Associated with the Absence of Spontaneous Conception

The median time to conception after medical treatment of EP was 14 months, with a minimum of 4 months and a maximum of 36 months; 30 pregnancies (73.2%) were carried to term, and vaginal delivery was the preferred mode of delivery (73.6%) (**Table 6**).

3.6.1. Univariate Analysis

Table 7 shows that women with a history of STI had 3 times the risk of

Table 3. Distribution according to gestational age, location and Fernandez score.

Variables	Size (N)	Percentage (%)
Gestational age (SA)		
<6]	26	37.1
[6 - 8]	35	50
[>8]	9	12.9
Side		
Left	34	48.6
Right	36	51.4
Location		
Ampullary	43	61.4
Infundibular	13	18.6
Isthmic	12	17.1
Interstitial	2	2.9
Fernandez score		
[6 - 7]	0	0
[7 - 12]	66	94.3
[13 - 18]	4	5.7

Table 4. Distribution according to methotrexate protocol and B-HCG kinetics.

Variables	Size (N)	Percentage (%)
Route of administration		
In-situ	0	0
Intramuscular	70	100
Method of administration		
Single dose	41	58.6
Multidose	29	41.4
Initial B-HCG		
[>5000]	13	18.6
[3000 - 5000]	4	5.7
[<3000]	53	75.7
B-HCG at D7		
[>4000]	2	3.4
[1000 - 4000]	20	34.5
[<1000]	36	51.4
Percentage reduction in B-HCG after 1 week (%)		
[<40]	13	22.4
[40 - 70]	25	43.1
[>70]	17	29.3
No reduction or increased	3	5.2

Table 5. Distribution according to spontaneous conception after medical treatment of EP.

Variables	Size (N)	Percentage (%)
Spontaneous Yes conception	41	58.6
No	29	41.4

Table 6. Average time to conception and other reproductive outcomes after medical treatment of EP.

Variables	Effectif (N)	Pourcentage (%)
Time to conception after treatment (months)		
<12]	7	17.1
[12 - 18]	26	63.4
>18]	8	19.5
Issue de la grossesse		
Recurrence of EP	6	14.6
Miscarriage	5	12.2
Premature delivery	0	0
Delivery at term	30	73.2
Mode of delivery		
Vaginal delivery	22	73.6
Cesaerian section	8	26.7

Table 7. Factors associated with the absence of spontaneous conception after univariate analysis.

Variables	Absence of spontaneous conception		OR (IC à 95%)	P
	N = 29; n(%)	N = 41; n(%)		
Delivery before EP				
Yes	13 (34.2)	25 (65.8)	0.52 (0.19 - 1.36)	0.137
No	16 (50.0)	16 (50.0)	1	
Endo-uterine manipulation				
Yes	12 (42.9)	16 (57.1)	1.10 (0.41 - 2.90)	0.519
No	17 (40.5)	25 (59.5)	1	
History of STI				
Yes	20 (54.1)	17 (45.9)	3.13 (1.15 - 8.54)	0.021
No	9 (27.3)	24 (72.7)	1	
History of tubal obstruction				
Yes	7 (100.0)	0 (0.0)	/	0.001

Continued

No	22 (34.9)	41 (65.1)		
SOPK				
Yes	4 (100.0)	0 (0.0)	/	0.026
No	25 (37.9)	41 (62.1)		
History of pelvic surgery				
Yes	5 (50.0)	5 (50.0)	1.50 (0.39 - 5.74)	0.397
No	24 (40.0)	36 (60.0)	1	
MTX protocol				
Single dose	13 (44.8)	16 (55.2)	1.27 (0.48 - 3.32)	0.405
Multidose	16 (39.0)	25 (61.0)	1	
EP Location				
Ampullary	19 (44.2)	24 (55.8)	1.34 (0.50 - 3.61)	0.368
Interstitial	0 (0.0)	2 (100.0)	/	0.340
Infundibular	4 (30.8)	9 (69.2)	0.56 (0.15 - 2.06)	0.294
Isthmic	6 (50.0)	6 (50.0)	1.52 (0.43 - 5.3)	0.363

Table 8. Independent factors associate with absence of spontaneous conception.

Variables	Absence of spontaneous conception		OR (IC à 95%)	Ajusted P
	N = 29; n (%)	N = 41; n (%)		
History of STI	20 (54.1)	17 (45.9)	2.22 (0.74 - 6.61)	0.151

not conceiving spontaneously after medical management of an EP ($p = 0.021$), after univariate analysis.

3.6.2. Multivariate Analysis

After multivariate analysis using the binary logistic regression method, we were unable to confirm that there was an association between a history of STIs and fertility prognosis (Table 8).

4. Discussion

The aim of our study was to evaluate the prognosis of subsequent spontaneous fertility of patients after medical treatment of tubal ectopic pregnancy in two hospitals in the city of Yaoundé. More specifically, we sought to describe the sociodemographic and clinical characteristics of patients who had undergone medical treatment for EP; to describe the different therapeutic protocols; to determine the spontaneous conception rate after medical treatment; and to report the mean time to conception after medical treatment for EP.

The mean age of our study population was 27.8 ± 3.81 years, which is similar to the result found by Kenfack *et al.* in Cameroon [6], who found a mean age of

26.46 ± 5.42 years. The most affected age group was [21 - 35] years, which is in the same line to what Dohbit *et al.* found in 2010 in Cameroon [7]. These similarities could be justified by the fact that the majority of our patients were single, had a higher level of education (mostly students) and that this predominant age group corresponds to a period of intense genital activity in women and to increased risky sexual behaviour in our context [8].

The past medical history of our patients revealed that 52.9% had a pelvic inflammatory disease and the most frequently germ found was Chlamydia trachomatis (47.1%). On the other hand almost 15% of our study population had already undergone surgery for EP. Assessing risk factors for ectopic pregnancy in a population of Cameroonian women, Assouni *et al.* found a 13-fold increased risk of developing an ectopic pregnancy in women with PID [9]. Similarly, in a retrospective cohort of 30,450 PID patients and 91,350 controls, Huang *et al.* found that PID patients had a 2.121-fold ($p = 0.003$) higher risk of developing an ectopic pregnancy in Taiwan region [10]. All these results are supported by Xia *et al.* who explored the relationship between chlamydia trachomatis infections and ectopic pregnancy in a recent meta-analysis and systematic review, and found that the association between chlamydia trachomatis infections and the risk of EP showed an odds ratio (OR) of 3.03, with a 95% confidence interval (CI) of 2.37 to 3.89 [11]. Our result is therefore in line with numerous studies that have identified PID as a major risk factor for EP, due to scarring leading to tubal obstruction that interferes with egg capture and migration.

The median Fernandez score was 11, with a minimum score of 4 and a maximum score of 13, which justified the choice of medical treatment for EP according to the score recommendations; the administration route of methotrexate was intramuscular (IM) in all our patients. This result is similar to that of Amélie Gervaise *et al.* [12] in 2004 in France, where the preferred administration route was intramuscular in 51.6% of cases. This is due to the non-invasive and easily achievable nature of IM injection; and the single-dose protocol was used most frequently in 58.6% of cases, which is similar to the results found by Silvia Baggio *et al.* [2] in 2021, where the single-dose protocol was used in 71.7% of patients with fewer side effects and a similar success rate to the multi-dose protocol [13] [14]. The initial B-HCG level was <3000 in 75.7% of cases and, at D7, this level was less than 1000 IU in 51.4% of cases, with a percentage reduction in B-HCG during the first week of between 40% and 70%.

After medical treatment of EP with MTX, we observed a spontaneous conception rate of 58.6% with a recurrence rate of EP of 14.6%. Several studies have reported similar results, with post-treatment conception rates ranging from 55% to 80% [2] [4] [5] [11] [12] [15]. In trials comparing the spontaneous conception rate after expectant management, medical treatment with MTX and surgery, the spontaneous conception rate after medical treatment with MTX was slightly lower than after surgery, but the recurrence rate of EP was significantly higher in

the surgery group. This suggests a better efficacy in terms of intrauterine pregnancy after medical treatment with MTX, certainly due to the non-invasive nature of the procedure and the almost complete absence of the risk of pelvic or intra-tubal adhesions associated with surgery.

5. Conclusion

The spontaneous fertility rate after medical management of EP was 58.6%, of which 73.2% were term pregnancies and 14.6% were recurrent ectopic pregnancies.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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