

Clinical Predictive Factors Affecting Laparoscopic Approach in the Management of Ectopic Pregnancy: A Retrospective Cross-Sectional Study

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Abstract

Introduction: Ectopic pregnancy accounts for approximately 2% of all pregnancies and is the most common cause of pregnancy-related mortality in the first trimester. Our aim was to study the preoperative clinical factors affecting the choice of laparoscopic approach to tubal ectopic pregnancy.

Materials and methods: This was a retrospective cross-sectional study of tubal ectopic pregnancy cases that were managed by laparoscopy at an academic university hospital in the period January 2010 to December 2018. Cases that were managed medically or conservatively and laparoscopic cases that were converted to laparotomy were excluded. Cases where the surgical approach of laparoscopy or laparotomy was determined by the patients' choice were also excluded.

Results: The laparoscopy rate was 49.4%. The mean age was 32.04 years. Compared with laparotomy, laparoscopy was significantly associated with low parity (less than 3) ($p=0.008$), a low level of initial beta-human chorionic gonadotrophin ($p=0.032$), fewer cases of adnexal mass ($p=0.000451$), hemoperitoneum ($p=0.000072$), ruptured ectopic ($p=0.000261$), and more cases of bowel adhesions ($p=0.0095$). There was no significant difference between laparoscopy and laparotomy regarding the risk factors of ectopic pregnancy. Salpingectomy and salpingostomy were not significantly different between the two surgical approaches ($p=0.643$). Twenty-eight laparoscopic cases were converted to laparotomy.

Conclusion: The laparoscopic approach to ectopic pregnancy was affected by parity, presenting symptoms of pain and vomiting, mean initial beta-human chorionic gonadotrophin, the presence of adnexal mass, the presence of hemoperitoneum, and the rupture of the ectopic. Bowel adhesions were seen more frequently in laparoscopy than in laparotomy. Salpingectomy and salpingostomy were no different between laparoscopy and laparotomy.

Keywords: Ectopic pregnancy, laparoscopy, hemoperitoneum, adnexal mass

(J Med J 2023; Vol. 57 (3): 236-245)

Received

Accepted

December 15, 2021

January 11, 2022

INTRODUCTION

Ectopic pregnancy accounts for approximately 2% of all pregnancies and is the

most common cause of pregnancy-related mortality in the first trimester [1].

The combination of ultrasound scan, beta-human chorionic gonadotropin (β -HCG), pregnancy testing, and laparoscopy has led to a rising incidence of diagnosed ectopic pregnancy prior to rupture [2]. Ectopic is, and will remain, a potentially life-threatening disease and must be approached as such [2].

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Bouyer et al. [3] found that 70% of tubal ectopic pregnancies were ampullary and complications and treatment depended on the site of the ectopic. In a review, Hajenius et al. [4] found that laparoscopic conservative surgery was associated with a higher persistent trophoblast rate than the open approach. There were similar tubal patency rates and comparable subsequent intrauterine pregnancies. These differences were not statistically significant.

Our retrospective cross-sectional study was conducted to evaluate the different preoperative clinical variables affecting the choice of surgical approach to ectopic pregnancy. We focused on laparoscopic management and compared it with laparotomy since the current evidence indicates no difference in terms of health benefits between laparoscopy and laparotomy, including the subsequent successful pregnancy [20].

MATERIALS AND METHODS

A retrospective cross-sectional study was conducted at Jordan University Hospital involving ectopic pregnancy cases in the period January 2010 to December 2018. Cases that were treated medically or conservatively, or laparoscopic cases converted to laparotomy, were excluded. The converted cases were not included since they could neither be counted as laparoscopy nor laparotomy. The data were obtained using patients' electronic and paper-based files. We searched clinic, emergency, and operative notes and collected data on demographics, risk factors (age, parity, previous miscarriages, previous ectopic pregnancies, smoking, previous tubal surgery, history of infertility and its treatment, previous pelvic inflammatory disease (PID), presenting symptoms, initial β -HCG levels, ultrasound scan (U/S) findings, operative findings and operative procedure(s).

The prevalence of both primary and recurrent ectopic pregnancy was identified. We evaluated and compared different features between cases managed by laparoscopy and those approached by laparotomy.

All operations were performed under general anesthesia. All patients were confirmed

to have ectopic pregnancies during surgery and later by histopathological report. Laparotomy was performed through either a transverse suprapubic incision (Pfannenstiel) or midline abdominal incision below the umbilicus. Laparoscopy was done with carbon dioxide (CO₂) insufflation and using a 10 mm umbilical trocar incision along with two 5 mm trocar incisions (one was suprapubic and the other in the left iliac fossa).

The study was approved by the institutional review board (IRB) at the hospital. For statistical analysis, we used XLSTAT and Data Toolkit as well as selected features of SPSS using the imported file. For all tests, both the Chi-square contingency and student *t*-test were used. A *p* value of <0.05 was considered significant.

RESULTS

Jordan University Hospital is a tertiary teaching hospital in Amman, the capital of Jordan. It has 5,000 deliveries annually. In the study period from January 2010 to December 2018, there were 206 surgical cases of ectopic pregnancies. We identified 178 ectopic pregnancy cases treated by laparoscopy or laparotomy. Of these, 164 were primary and 14 recurrent. Twenty-eight laparoscopic cases were excluded because they had been converted to laparotomy due to the lack of an experienced laparoscopist.

There was no difference in the mean age between laparoscopy and laparotomy-treated patients, both for each age group and cumulatively. The mean age was 32.04 and 32.3 for the laparoscopy and laparotomy, respectively. A Chi-square test was also performed for age groups ($p=0.728617$), suggesting that age does not affect the type of surgery.

Concerning parity, after collapsing the data, we found a statistical significance in the Chi-square test when patients were grouped as low parity (<3) vs high parity (≥ 3). Post-hoc values showed that significantly more patients (30%) with parity ≥ 3 underwent laparotomy rather than laparoscopy ($p=0.008$). The relative risk (RR) was also calculated to be 1.665 (95%

confidence interval–CI) (1.156–2.400). Women with parity <3 were almost 1.7 times more likely to undergo laparoscopy than those with parity ≥ 3 .

No significant difference was found between previous history of miscarriages and type of surgery. The different demographic characteristics are shown in Table 1.

Table 1: Demographic characteristics

	Treated by		Statistics
Age (years)	Laparoscopy	Laparotomy	<i>t</i> -test <i>p</i> value
<20	0	1	N/A
20–29	26	28	0.948
30–39	56	51	0.834
≥ 40	6	10	0.212
Parity (P)			
P0	24	21	
<P3	41	26	<i>p</i> =0.008
$\geq P3$	23	43	
Previous miscarriages			Chi-square test
0	45	46	<i>p</i> =0.928
<3	30	29	not significant at <i>p</i> <0.05
≥ 3	13	15	

A previous history of ectopic pregnancy was not found to affect the choice of the type of surgery.

The Chi-squared test was inconclusive for smoking since there were only two laparoscopy-treated smokers and no laparotomy-treated patients. Treatment by laparoscopy was 2.1 times more likely for smokers than non-smokers. This result was a weak correlation, RR 2.059 and CI (1.768–2.398).

A history of previous tubal surgery was not relevant in comparison between the two types of surgical operations, RR 1.417, CI (0.691–2.908). A history of infertility and assisted reproduction,

including in vitro fertilization (IVF), was not found to affect the type of surgery.

The Chi-squared test was inconclusive for the history of pelvic inflammatory disease (PID) because no cases were reported in the laparoscopy group, and only one case in the laparotomy group.

Of the 20 patients who used an intrauterine contraceptive device (IUCD), nine had undergone a laparoscopy and 11 a laparotomy. The Chi-square statistic with Yates' correction was calculated. Use of an IUCD was not found to affect the choice of surgery (*p*=0.897). Table 2 shows the risk factors of ectopic pregnancy with their effect on the choice of surgery.

Table 2: Risk factors for ectopic pregnancy

	Treated by		Chi-square with Yates correction	RR	95% CI
Previous ectopic pregnancy	Laparoscopy	Laparotomy	<i>p</i> value		
Primary cases	83	81	0.429	1.417	0.691–2.908
Recurrent cases	5	9			
Smoking			Chi-square test		
Smoker	2	0	Inconclusive Chi-square test	2.059	1.768–2.398
Non-smoker	85	90			
Previous tubal surgery			Chi-square with Yates correction		
Yes	6	6	<i>p</i> =0.796	1.012	0.563–1.819

	Treated by		Chi-square with Yates correction	RR	95% CI
No	82	84			
History of infertility			Chi-square with Yates correction		
Yes	14	13	$p=0.924$,	1.065	0.715–1.588
No	73	77			
IVF-assisted reproduction			Chi-square with Yates correction		
Yes	7	5	$p=0.734$	1.196	0.723–1.977
No	81	85			
History of PID			Chi-square test		
Yes	0	1	Inconclusive Chi-square test	0.503	0.045–5.571
No	88	89			

Regarding the presenting symptoms, 70.6% of women who had no pain underwent laparoscopic surgery (41% more than those who underwent laparoscopy), while 56% of women presenting with pain underwent laparotomy. Patients who were not in pain were 1.6 times more likely to undergo laparoscopic surgery than those who presented with pain, RR 1.602 and 95% CI (1.205–2.131).

Vomiting was also found to affect the type of surgery. 91% of women who vomited were treated with laparotomy. There was only a 3% difference

in treatment between patients who did not vomit. However, using the relative risk statistics, the difference in choice of surgery was considered insignificant, RR 0.177, 95% CI (0.027–1.15).

Vaginal bleeding, shoulder-tip pain, syncope and diarrhea were found to have insignificant differences between laparoscopy and laparotomy cases. Table 3 shows the varying presenting symptoms of ectopic pregnancy with their effect on the type of surgical management.

Table 3: Presenting symptoms

	Treated by		Statistics	RR	95% CI
Pain	Laparoscopy	Laparotomy	Chi-square with Yates correction		
Yes	63	80	$p=0.009$	1.602	1.205–2.131
No	24	10			
Vomiting			Chi-square with Yates correction		
Yes	1	10	$p=0.016$	0.177	0.027–1.15
No	85	80			
Bleeding			Chi-square with Yates correction		
Yes	68	77	$p=0.279$	0.790	0.565–1.104
No	19	13			
Diarrhea			Chi-square		
Yes	0	4		0.200	0.014–2.785
No	86	86	Inconclusive due to 0 value		
Shoulder-tip pain			Chi-square with Yates correction		
Yes	2	9	$p=0.070$	0.355	0.101–1.255
No	85	81			
Syncope			Chi-square		
Yes	0	4		0.200	0.014–2.785
No	86	86	Inconclusive due to 0 value		

There was a statistically significant difference between mean initial β -HCG levels in laparoscopy vs laparotomy patients ($p=0.032$). Mean initial β -HCG level was 2838 mIU/ml and 7708 mIU/ml in laparoscopy vs laparotomy patients, respectively. For the subgroup of patients with β -HCG <1500 mIU/ml, there were 43 cases in the laparoscopy and 37 cases in the laparotomy with no statistically significant difference ($p=0.323$). For β -HCG >6500 mIU/ml, there were ten cases in the laparoscopy and 17 cases in the laparotomy, with no statistically significant difference. There was no statistical significance in the difference between means of gestational age in laparoscopy vs laparotomy treated patients (6.5 weeks vs 6.27 weeks, $p=0.505$).

Of the preoperative U/S scan findings, only the presence of an adnexal mass and evidence of hemoperitoneum were found to have a statistically significant influence on the type of surgery (RR 1.782, CI (1.284–2.472) and RR 2.129, CI (1.405–3.228), respectively).

Sixty-four per cent of patients with an adnexal mass underwent laparotomy, while 64% of patients without a mass underwent laparoscopy. Regarding the preoperative U/S scan finding of hemoperitoneum, 71% of women whose scans detected evidence of hemoperitoneum underwent laparotomy; in contrast, 62% of women whose scans did not detect any evidence of hemoperitoneum underwent laparoscopic surgery (Table 4, Chi-square with Yates correction, RR and 95% CI).

Table 4: Preoperative scan findings

	Treated by		Statistics		
	Laparoscopy	Laparotomy	<i>p</i> value	RR	95% CI
Detection of ectopic					
Yes	51	53	0.876	0.953	0.704–1.29
No	35	33			
Adnexal mass seen					
Yes	30	54	0.000451	1.782	1.284–2.472
No	56	32			
Empty uterus					
Yes	74	76	0.819	0.904	0.598–1.369
No	12	10			
Free fluid in POD					
Yes	40	50	0.169	0.792	0.587–1.07
No	46	36			
Evidence of hemoperitoneum					
Yes	18	44	0.000072	2.129	1.405–3.228
No	68	42			
Gestational sac seen					
Yes	11	16	0.402	0.788	0.487–1.275
No	75	70			
Fetal heart activity					
Yes	5	7	0.765	0.823	0.414–1.636
No	81	79			
Endometrial status					
Thickened	23	18	0.090	2.805	0.789–9.976
Thin	2	8			

POD: Pouch of Douglas

Concerning the operative findings (Table 5), the size and site of the ectopic mass were not

found to differ significantly between the laparoscopy and laparotomy patients.

Table 5: Operative findings

	Treated by		Statistics		
Size of mass (max. diameter)	Laparoscopy	Laparotomy	Chi-square test	RR	95% CI
<2 cm	2	1	$p=0.199$		
2–5 cm	28	29			
>5 cm	1	1			
Unknown due to rupture	11	27			
Tubal pregnancy			Chi-square test		
Left tubal	36	48	$p=0.085$		
Right tubal	50	37			
Non-tubal ectopic pregnancy	2	5			
Rupture			Chi-square test with Yates correction		
Yes	12	35	$p=0.000261$	2.272	1.365 - 3.782
No, intact	76	55			
Presence of adhesions			Chi-square test		
No	70	74	$p=0.195$	1.089	0.761 - 1.559
Yes	18	16			
If yes, type of adhesions present			Chi-square test with Yates correction		
Involving tubes and ovaries	3	7			
Involving bowel	11	6	$p=0.0095$		
Hepatic	2	0			
Uterus to abdominal wall	2	3			
Presence of hemoperitoneum			Chi-square test with Yates correction		
No	42	25	$p=0.0095$	1.513	1.134 - 2.018
Yes	46	65			
If yes, volume of hemoperitoneum			Chi-square test with Yates correction		
<150 cc (not 0)	15	9	$p=0.0208$	1.852	1.197 - 2.865
150–300 cc	13	18			
>300 cc	14	35			
Presence of contralateral pathology			Chi-square test with Yates correction		
Yes	11	15	$p=0.565$	0.835	0.519 - 1.344
No	77	75			

Out of the total number of tubal ectopic pregnancies, left and right accounted for 50% each.

Ruptured ectopic pregnancies were seen more in the laparotomy approach, RR 2.272 and

95% CI (1.365–3.782). Of ruptured ectopic pregnancies, 74% were treated by laparotomy and 58% of intact ectopic pregnancies were treated by laparoscopy.

Overall, the presence of adhesions was not found to be significantly different between the two types of surgery. However, adhesions involving the bowel were more significantly associated with laparoscopy than laparotomy ($p=0.0095$).

The presence of hemoperitoneum was found to be more significantly associated with laparotomy. Some 63% of patients who did not have hemoperitoneum were treated by laparoscopy ($p=0.0095$; RR 1.513; 95% CI [1.134–2.018]). Of those with hemoperitoneum, 59% were treated by laparotomy.

The volume of hemoperitoneum was also correlated with the type of surgical approach; 63% of patients with hemoperitoneum of <150 cc were treated by laparoscopic surgery and 66% of patients with hemoperitoneum of >150 cc were treated by laparotomy ($p=0.0208$; RR 1.852; 95% CI [1.197–2.865]). The presence of contralateral pathology was not found to be different between the two types of surgical approaches (Table 5).

We compared the two surgical procedures (salpingectomy and salpingostomy) performed in the laparoscopy and laparotomy and found no statistically significant difference ($p=0.643$). Salpingectomy was performed in 73 cases of laparoscopy and 72 cases of laparotomy. Salpingostomy was performed in 15 laparoscopic cases and in 19 laparotomy cases.

DISCUSSION

The overall rate of ectopic pregnancy in Jordan is still relatively low. This hospital is a large teaching hospital in the capital Amman. Annually, there are around 22.9 cases of surgically managed ectopic pregnancies at this hospital. In the UK, the incidence is approximately 11/1000 pregnancies with an estimated 11,000 ectopic pregnancies per year [5].

In our study, low parity was found to be significantly associated with laparoscopic management as these women were usually highly educated and their age was relatively older than the laparotomy group. Most of our patients were in the age group 30–39 years. Other studies found a mean age for patients with ectopic pregnancy at 31 years [6] and 30.4

years [7]. These were very similar to our results.

Jacob et al. [7] found that previous ectopic pregnancy and previous genital surgery were strongly associated with ectopic pregnancy. In addition, they found that psychiatric diseases had an additional impact on the risk of ectopic pregnancy. Assouni Mindjah et al. [8] identified some new risk factors, including smoking at the time of conception. In our study, history of previous miscarriage and presence or absence of risk factors (such as previous ectopic pregnancy) for ectopic pregnancy were not found to affect the choice of surgical approach.

In our study, the presenting symptoms of pain and vomiting were respectively significantly associated with laparotomy due to pressure incurred on the treating gynecologists by the patients and their families, making them rush to laparotomies.

Laparoscopy was also associated with low initial β -HCG both mean and the subgroup of <1,500 mIU/ml. Moreover, U/S detection of hemoperitoneum and adnexal mass was seen to be significantly associated with laparotomy. These features usually favored a conservative approach towards laparoscopy [9].

Our laparoscopy rate was 49.4% (88 patients), which was much higher than a previous report from the north of Jordan, where most of the cases were ruptured ectopics [10].

We used a combination of β -HCG and transvaginal U/S scan to diagnose ectopic pregnancy, a combination which has been shown to have a sensitivity of 97% and a specificity of 95% [11].

Adhesions involving the bowel were significantly more in the laparoscopy than laparotomy as laparoscopy has the advantage of being able to visualize the whole abdomen and pelvis. Among the laparoscopy patients, the prevalence of adhesions was 20% and the overall rate of adhesions was 19%. There were only two cases with perihepatic adhesions in the laparoscopic patients and none in the laparotomy patients as it was difficult to visualize the perihepatic surfaces in laparotomy. Mullins et al. [12] found that among 802 patients with ectopic pregnancy managed surgically, 7.5% were found to have

perihepatic adhesions. In all our patients, adhesions involving the tubes and ovaries were only seen in ten cases (5.6%), much lower than the finding of Horn et al. [13] that 50% of ectopic pregnancies had evidence of tubal pathologies. However, Horn et al. included both adhesions and inflammation in their tubal disease, while we only included clinical adhesions.

Salpingectomy was performed for most of the patients with no difference between the laparoscopy and laparotomy. The practice in our hospital was to perform salpingectomy if the contralateral tube was normal. This practice was in line with the results of a multicenter randomized controlled trial [14], which concluded that in women with a tubal ectopic pregnancy and a healthy contralateral tube, salpingotomy does not significantly improve fertility prospects compared with salpingectomy. Cases of salpingostomy were followed up with β -HCG as the risk of persistent trophoblastic disease is a primarily associated with salpingostomy, in line with NICE recommendations [15]. Moreover, salpingectomy had no significant effect on ovarian reserve [16].

The salpingostomy cases were performed for small unruptured cases in both laparoscopy and laparotomy, all without suturing. Fujishita et al. found that suturing had no additional benefit over non-suturing during salpingotomy [17]. In contrast, Li et al. [18], in a retrospective study concluded that suturing after laparoscopic salpingotomy can decrease the tubal damage and recover its normal structure.

In our study, the choice of the surgical approach and procedure was influenced by different preoperative variables. Twenty-eight laparoscopic cases were converted to laparotomy due to the unavailability of an experienced laparoscopic surgeon. Jennifer et al. [19] found substantial variation in the management of ectopic pregnancy with significant racial and insurance influences.

Our laparotomy rate was higher than that of laparoscopy (50.6% vs 49.4%). There was no difference in terms of health benefits between

laparoscopy and laparotomy, including the key outcome of a subsequent successful pregnancy [15]. Saranovic et al. [20] found that tubal patency and the number of intrauterine pregnancies after laparoscopic surgical treatment were no higher than after treatment by laparotomy.

CONCLUSION

A laparoscopic approach to ectopic pregnancy was affected by parity, presenting symptoms of pain and vomiting, mean initial β -HCG, the presence of adnexal mass, the presence of hemoperitoneum, and rupture of the ectopic. The presence of bowel adhesions was seen more frequently in laparoscopy than laparotomy. Salpingectomy and salpingostomy were no different to laparoscopy and laparotomy.

List of abbreviations

β -HCG: beta-human chorionic gonadotrophin
IUCD: intrauterine contraceptive device
POD: Pouch of Douglas
 p value: probability value
U/S: ultrasound scan
CO₂: carbon dioxide
IRB: institutional review board
IVF: in vitro fertilization
PID: pelvic inflammatory disease
RR: relative risk
CI: confidence interval

DECLARATIONS

Ethics approval and consent to participate: the study obtained approval of the IRB at Jordan University Hospital. Consent to participate was not applicable.

Consent for publication: not applicable.

Availability of data and materials: the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: the authors declare that they have no competing interests.

Funding: this study received no funding in any form.

Acknowledgements: none.

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العوامل التنبؤية السريرية التي تؤثر على النهج بالمنظار في علاج الحمل خارج الرحم؛ دراسة مستعرضة بأثر رجعي

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الملخص

الخلفية والأهداف : يمثل الحمل خارج الرحم حوالي 2% من جميع حالات الحمل وهو السبب الأكثر شيوعاً للوفيات المرتبطة بالحمل في الأشهر الثلاثة الأولى. هدفنا هو دراسة العوامل السريرية قبل الجراحة التي تؤثر على اختيار النهج بالمنظار للحمل خارج الرحم البوقي .

المنهجية : هذه دراسة مستعرضة بأثر رجعي لحالات الحمل خارج الرحم البوقي التي تم علاجها بالمنظار في مستشفى جامعي أكاديمي في الفترة الممتدة من يناير 2010 إلى ديسمبر 2018. تم استبعاد الحالات التي تم علاجها طبياً (باستخدام الأدوية) أو تحفظياً وحالات العلاج بالمنظار التي تم تحويلها إلى فتح البطن. كما تم استبعاد الحالات التي تم فيها تحديد النهج الجراحي لتنظير البطن أو فتح البطن بناء على اختيار المرضى.

النتائج: كان معدل حالات تنظير البطن 49.4%. كان متوسط العمر 32.04 سنة. بالمقارنة مع فتح البطن، ارتبط التنظير بشكل كبير بانخفاض عدد الولادات السابقة (أقل من 3) (القيمة الاحتمالية 0.008)، وانخفاض مستوى هرمون الغدد التناسلية المشيمية البشرية بيتا (القيمة الاحتمالية 0.032)، وحالات أقل من الكتل في ملحقات الرحم (القيمة الاحتمالية 0.000451)، تدمي الصفاق (القيمة الاحتمالية 0.000072)، تمزق الحمل خارج الرحم (القيمة الاحتمالية 0.000261)، ولكن المزيد من حالات التصاقات الأمعاء (القيمة الاحتمالية 0.0095). لم يكن هناك فرق كبير بين تنظير البطن وفتح البطن فيما يتعلق بعوامل الخطر للحمل خارج الرحم. لم يكن استئصال البوق وفغر البوق مختلفين بشكل كبير بين النهجين الجراحيين (القيمة الاحتمالية 0.643). تم تحويل ثمانية وعشرين حالة بالمنظار إلى فتح البطن.

الاستنتاجات: تأثر النهج بالمنظار للحمل خارج الرحم بعدد الولادات السابقة، والقولم بأعراض الألم والقيء، معدل مستوى هرمون الغدد التناسلية المشيمية البشرية بيتا الأولي، وجود كتل في ملحقات الرحم، وجود تدمي الصفاق وتمزق الحمل خارج الرحم. شوهد وجود التصاقات الأمعاء بشكل متكرر في حالات تنظير البطن أكثر من فتح البطن. لم يكن استئصال البوق وفغر البوق مختلفين بين تنظير البطن وفتح البطن.

الكلمات الدالة: خارج الرحم، الحمل، تنظير البطن، تدمي الصفاق، كتل ملحقات الرحم.