

## Setting priorities in the conventional approaches in managing ectopic pregnancy; is it time to reform? A teaching hospital experience

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### Abstract

**The aim of the study:** To review the management approaches of ectopic pregnancy (EP) at the Department of Obstetrics and Gynecology at Jordan University Hospital (JUH).

**Material and methods:** All patients admitted to our department with the diagnosis of EP treated during the study period extending from January 2017 to June 2019. Data were collected retrospectively using the patients' files anonymously. Main outcome measures: age, parity, ectopic site, presentation, the main risk factor/s and the management plan.

**Results:** In total, 65 cases of EP were managed during the study period. Overall, the mean age was 30 years. EP was located in the right tube in 23 cases, and in the left tube in 14 cases. Eleven patients presented with acute abdomen due to rupture of the EP and underwent urgent laparotomy; 7 of these cases were located on the right side. Conservative surgery (laparoscopy versus laparotomy) was the main line of management with attention to preserving the tube patency, followed by medical therapy when the patient fulfilled the criteria or those with pregnancy of unknown location.

**Conclusions:** EP is a life-threatening condition. It is time to reform the priorities in the conventional approach to management. Every effort ought to be applied to preserve the reproductivity of women who are diagnosed with EP at the JUH. We would suggest that salpingostomy needs to be considered the surgical treatment of choice for the majority of these cases.

**Key words:** ectopic pregnancy, pregnancy of unknown location, salpingostomy.

### Introduction

An ectopic pregnancy (EP) is a pregnancy located outside the uterine cavity. The reported incidence of EP in the literature is 1.5% to 2% [1]. With increase in *in vitro* fertilization, the incidence rises to 2.5- to 5-fold [2]. The most common complication of ectopic pregnancy is rupture, which occurs in 15-20% of ectopic pregnancies [3]. When ruptured, it is a true surgical emergency, being the leading cause of maternal mortality in the first trimester of pregnancy and accounting for 4% of all maternal deaths [4]. There seems to be a great deal of controversy, extending from the etiology of the implantation to its clinical management as it is still relatively unclear why the fertilized embryo stops and develops in the Fallopian tube instead of the uterine cavity.

There is also no consensus regarding the ideal method of management. Although fallopian tube EP has the highest rate among all ectopics (96%) [5], other possible sites include cervical, interstitial, hysterotomy

scar, intramural, ovarian, or abdominal. In addition, in rare cases of multiple gestation it may be heterotopic (including both a uterine and extrauterine pregnancy) [6]. Nevertheless, EP is a potentially life-threatening condition and currently the leading cause of pregnancy-related deaths during the first trimester, accounting for 10% of all maternal deaths [7, 8]. There is a dilemma regarding the best approach of management as there appears to be much controversy surrounding this essential step. The discussion focuses initially on the choice of medical versus surgical treatment. While surgical approaches are the gold-standard treatment, advances in early diagnosis in the 1980s facilitated the introduction of medical therapy with methotrexate [9]. With the routine use of early ultrasound, the diagnosis of ectopic pregnancy can be established early and medical treatment can be administered in many cases. The overall success rate of medical treatment in properly selected women is nearly 90% [10]. With a surgical approach there is a need to address the question of whether to

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perform a laparoscopy or a laparotomy. Lastly, if surgery is undertaken, should salpingectomy or salpingostomy be performed? On balance, salpingostomy should probably be the surgical treatment of choice for the majority of women with ectopic pregnancy, as a study has found that after adjusting for any confounding factors, the incidence of ectopic pregnancy was significantly associated with decreased ovarian reserve [6]. In selected cases of early ectopic pregnancy or pregnancy of unknown location, expectant management is an option. In this paper, we present the results of our experience in the Department of Obstetrics and Gynecology at the University of Jordan, especially since there are no clear departmental guidelines for dealing with these cases, and the choice is dependent on personal experience and the recommendations of medical schools endorsed by the consultant himself.

### Material and methods

This is a retrospective study including all patients admitted to the Department of Obstetrics and Gynecology at Jordan University Hospital in Amman with the diagnosis of EP who were treated during the study period from January 2017 to June 2019. The exclusion criteria were patients who did not comply with the advised management, patients who did not have a follow-up, and patients who were managed in other hospitals. The study was carried out after the approval of the Insti-

tutional Review Board (IRB), the Ethics Committee and the Scientific Research Committee (SRC) at the Jordan University Hospital. All patients with the initial diagnosis of pregnancy of unknown location or EP were included in this study. Data analysis was done using the Statistical Package for the Social Sciences (SPSS). A total of 65 patients were treated for EP; the mean age of the women was 30.3 years (range 21-43 years) ( $\pm$ SD), the gravidity mean was 3.7 (range 1-9) ( $\pm$ SD) while the parity ranged from 0 to 4 with an average of 1.3 ( $\pm$ SD) as seen in Table 1. The site of EP was on the right tube in 23 (35.38%) patients, the left tube in 16 (24.62%) patients, unknown location in 7 (10.77%) patients, ruptured EP in 11 (16.92%) patients, bilateral EP in 2 (3.07%) patients and 6 (9.23%) patients presented with EP at the site of a previous cesarean scar incision as illustrated in Table 2. The condition of the EP was intact in 54 (83.70%) patients, ruptured in 11 (16.92%) patients, as illustrated in Table 3. A hard work aiming to sum up the predisposing factors for this abnormal pregnancy was carried out, and yielded the following as illustrated in Table 4: advanced maternal age and the presence of pelvic inflammatory disease (PID) were noted in 40 and 18 patients respectively. Smoking was also identified as a cofactor in 27 patients. For those of unknown location, the confirmation of empty uterus by detailed vaginal ultra-sonography was established, and positivity of  $\beta$ -hCG to confirm pregnancy. Admission to the hospital, full detailed history including the

**Table 1.** Distribution of patients by age

Age/years	Number	Percentage
21-25	11	16.92
26-30	14	21.54
31-35	21	32.31
36-40	10	15.38
41-45	9	13.85
Total	65	100

**Table 2.** Location of ectopic pregnancy

Site	Number	Percentage
Right tube	23	35.38
Left tube	16	24.62
Ruptured	11	16.92
Unknown	7	10.77
Previous scar	6	9.23
Bilateral	2	3.08
Total	65	100

**Table 3.** Condition of EP at time of presentation

Condition	Number	Percentage
Intact	54	83.08
Ruptured	11	16.92
Total	65	100

**Table 4.** Main risk factors

Risk factor	Number
Previous ectopic pregnancy	6
Pelvic inflammatory disease and other genital infections	18
In vitro fertilization	4
Other assisted reproduction methods	5
Smoking	27
Increasing maternal age	40
Tubal reconstructive surgery	1
Infertility	7
Contraceptive methods	10
Others	3

main risk factors for the possibility of EP, and full clinical examination were performed. Routine blood tests were drawn including CBC, cross matching, and kidney function tests. Patients diagnosed with a ruptured EP based on history, physical findings and ultrasound evaluation showing a large amount of blood/fluid inside the pelvi-abdominal cavity and most of the hemodynamically unstable patients were transferred immediately to the operating theatre. Of the patients diagnosed with a pregnancy of unknown location, 5 underwent medical therapy and the remaining two underwent diagnostic laparoscopy where the location was not established, and subsequently underwent medical therapy. Four patients with a pregnancy at the site of a previous cesarean section scar were added to the medical group, and the rest of the patients in the study underwent diagnostic laparoscopy  $\pm$  laparotomy according to the situation. Only two patients, who were diagnosed to have right tubal EP with low level of  $\beta$ -hCG, underwent expectant management by follow-up without interference. Bilateral EP, diagnosed in 2 patients, was approached with minilaparotomy and salpingostomy. After a thorough discussion with the patient about her case, the proper advice that suited her condition was offered and written consent obtained.

## Results

Urgent laparotomy was performed for those patients who presented with ruptured EP and were unstable. With an average amount of blood found in the pelvic cavity of 700 to 1500 cc ( $\pm$ SD), evacuation of the blood, identification of the site of bleeding and suturing were done. Furthermore, salpingectomy was performed in 7 patients and salpingostomy in 4 patients. The decision was taken by the operator based on his experience and judgment of the operative findings. Deciding to undergo diagnostic laparoscopy – which is the gold standard method – to confirm the diagnosis, further management was determined by the operator based on previous experience and the findings during the laparoscopic procedure. The process was completed laparoscopically in 13 (20.00%) patients or via a minilaparotomy in 8 (12.31%) patients. There are two surgical approaches for tubal pregnancy: either salpingectomy or salpingostomy. Traditionally, salpingectomy has been the standard procedure, but salpingostomy provides a conservative alternative option when possible, mainly for fertility purposes. Salpingostomy was the procedure of preference in 41 (63.07%) patients. Change is said to be the only constant. However, changing trends towards the conservative surgical approach entailing salpingostomy when possible instead of salpingectomy has been strongly opposed by a long-standing protocol of radical surgical treatment at our department and many other centers. For those patients

diagnosed with EP at the site of a previous scar, medical therapy with methotrexate was scheduled because it fulfilled the criteria of this type of therapy according to the well-known protocols: hemodynamically stable, no contraindications to MTX therapy, serum  $\beta$ -hCG concentration  $\leq$  5000 mIU/ml, no fetal cardiac activity detected on transvaginal ultrasound, and willingness and ability to comply with post-treatment follow-up and with access to emergency medical services within a reasonable timeframe in case of a ruptured fallopian tube. The 2 patients in the unknown location group who underwent diagnostic laparoscopy, in which no location could be identified during the procedure, were excluded from the study. The 2 patients diagnosed to have bilateral EP per their histopathological testing underwent minilaparotomy and bilateral salpingostomy. The 2 patients diagnosed to have right tubal EP with a low level of  $\beta$ -hCG underwent conservative therapy without surgical interference.

## Discussion

In our study, conservative treatment with its different modalities was an attractive choice that can be applicable in certain stabilized cases. Medical management with methotrexate is an alluring choice to avoid the conduit of surgery when its application is possible. From 11 (16.92%) patients treated under this category, 8 of them completed the plan successfully, while 3 patients developed complications that stipulated surgical interference. It is without a doubt worth mentioning that both conservative methods applied in our study group served our aim to maintain fertility of the patients and to avoid potential surgical complications. The patients received information on the risk of tubal rupture and the need for close surveillance. It should be emphasized, while employing this mode of treatment, that painstaking monitoring by the physicians is a key to successful treatment.

One must remain mindful of both the advantages and limitations of the different modalities in the management of ectopic pregnancy and when it is appropriate to use a specific treatment. Advances in the early diagnosis of pregnancy itself, and of abnormal pregnancy, combined with an increased awareness of the possibility of EP by gynecologists have changed the spectrum of EP remarkably during the past 20 years [11, 12]. The increased risk of EP is fueled not only by the epidemic of pelvic inflammatory disease, but also by the increased use of new reproductive procedures, such as embryo transfer and in vitro fertilization [13, 14]. Recently, there has been a major shift in our philosophy of management of EP from being drastic towards conformist, whether it should be a surgical or medical treatment. Our viewpoint in our practice when there is a suspicion of pregnancy is to localize the site

of pregnancy, and if found to be ectopic, to take the decision of management approach – surgical, medical, or conservative treatment – with the exception of cases of life-saving emergencies when there is a suspicion of ruptured EP. We are convinced of our therapeutic approach for the management of EP and to work on its application in the current study, as illustrated in the results section. We have made a strong effort to maintain women's reproductive capacities as we preserved the affected tubes in 37 (56.92%) patients, while in 19 (29.23%) patients it was necessary to proceed to the radical modality. As unfortunate as it may seem to be, this high percentage of patients undergoing the radical approach falls far from our aim and expectations. However, it could be explained by having these decisions made by coworkers with opposing opinions at the department.

Our current conservative approach towards EP summarized by our accumulated experience is also excellently appreciated by Leach and Ory in their review as they stated: "Surgical treatment remains the standard approach to manage EP" [15]. In reality, our aim towards this rising disease converted from the diagnosis of unruptured EP and unattainability to possible and even mandatory early interference. Worth mentioning here is our aim to overcome this point and to shift attention from reducing mortality towards safeguarding fertility, in line with a cultural desire to keep the family relationship in an ideal situation. All patients diagnosed to have a ruptured EP underwent urgent surgical intervention via a minilaparotomy to control the source of bleeding that jeopardizes the life of the patient together with evacuation of the hematoma and preservation of the ruptured tube if possible. Our view was in line with the other studies concerning this subject [16-19]. The pronouncement for running tubal ectopic pregnancy should be directed by the preliminary clinical figures and the dialogue of the paybacks and the jeopardies of each approach.

Disrupted anatomy, whether due to PID, previous surgery, using assisted reproductive techniques or any of the known factors listed in Table 4, has been identified as a major risk factor for the occurrence of EP in our practice and the current study. The distortion is often accompanied by functional impairment due to compromised ciliary function. These factors, along with the increased rate of EP among older women, explains the complex interaction between multiple risk factors in the same patient over a timeline. Smoking also plays a role in the occurrence of EP: ciliary damage, impaired tubal motility, and suppressed immunity, which could be a causative factor for PID. Smoking was identified in 27 (41.54%) patients in our study, in agreement with previous literature linking current smoking with a 2- to 3-fold increase in EP rate [20, 21]. We must remember that a woman with the aforementioned surgically pick-

led ectopic pregnancy is at higher risk for many obstetric complications in the subsequent pregnancies such as preterm birth, low birth weight, preeclampsia and many other complications of pregnancy. This should be taken into consideration in the management plan in the future pregnancies that need more frequent prenatal visits and monitoring particularly in the third trimester. We are convinced of the value of the great benefit for this group of patients as a result of closer care throughout the pregnancy period, as they are among the category of patients classified as a high-risk pregnancy in order to prevent harmful complications that can be avoided. Our current vision is congruent with others [22].

Since the guidelines concerning the management of EP are still of no consensus it is considered a limitation of the study. With no strict guidelines the management will depend mostly on the physician's preferences, which may have had an impact on the outcome of this study. Even though this is a concern, the patients included in the study were successfully treated. Additionally, the low number of patients is considered a limitation of the study. In future studies more patients should be included to strengthen the outcome of the study. This will be helpful in improving the practices and to standardize the guidelines. Another limiting factor in our study is the rarity of other uncommon types of ectopic pregnancy, e.g. cervical ectopic pregnancies. A strength of the study is that it summarizes extensive reviews of the management of EP. It also highlights the need for a standardized approach in the management of EP. Furthermore, it is of great help for the health personnel to provide the patients and their caregivers with all information needed to enable them to make an informed decision.

## Conclusions

Even though the incidence of EP is growing, not enough attention is being paid for this foremost issue that endangers the life of women. Early detection and awareness of EP is the hallmark of diagnosis within the locus of pregnancy findings which considerably leads to reduction of mortality, morbidity, and complications. The major test of medical skills is the remedial intervention and its timing, which are the key steps to maintaining the reproductive potential of women. Our study exhibits the application of laparoscopy for diagnosis and treatment, with a narrow window for the possibility of minilaparotomy as a backup to safeguard the function of the tubes for maintaining the reproductive capacity of women. The reproductivity of patients should be set as a second priority just after saving their lives when necessary. We conclude that salpingostomy as a treatment approach should always be thought of as the main therapeutic approach to maintain the wom-

an's reproductive capacity. Medical and conservative approaches are appealing substitutes in selected cases under the condition of guaranteed close follow-up. Programs of awareness dispersal about this intimidating abnormal pregnancy should be a core element in health establishment protocols.

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### Disclosure

The authors report no conflict of interest.

### References

- Bronson R. Ectopic pregnancy – still a challenge. *Fertil Steril* 2018; 110: 1265-1266.
- Ashraf M, Reihaneh H, Nadia J, et al. Risk factors for ectopic pregnancy: A case-control study. *J Res Med Sci* 2014; 19: 844-849.
- Lee R, Dupuis C, Chen B, et al. Diagnosing ectopic pregnancy in the emergency setting. *Ultrasonography* 2018; 37: 78-87.
- Berg CJ, Callaghan WM, Syverson C, Henderson Z. Pregnancy-related mortality in the United States, 1998 to 2005. *Obstet Gynecol* 2010; 116: 1302.
- Bouver J, Coste J, Fernandez H, et al. Sites of ectopic pregnancy: a 10-year population-based study of 1800 cases. *Hum Reprod* 2002; 17: 3224-3230.
- Alkatout I, Honemeyer U, Strauss A, et al. Clinical diagnosis and treatment of ectopic pregnancy. *Obstet Gynecol Surv* 2013; 68: 571-581.
- Kirk E, Bottomley C, Bourne T. Diagnosing ectopic pregnancy and current concepts in the management of pregnancy of unknown location. *Hum Reprod Update* 2014; 20: 250-261.
- Chouinard M, Mayrand MH, Ayoub A, et al. Ectopic pregnancy and outcomes of future intrauterine pregnancy. *Fertil Steril* 2019; 112: 112-119.
- Hackmon R, Sakaguchi S, Koren G. Effect of methotrexate treatment of ectopic pregnancy on subsequent pregnancy. *Can Fam Physician* 2011; 57: 37-39.
- Silva PM, Araujo Júnior E, Cecchino GN, et al. Effectiveness of expectant management versus methotrexate in tubal ectopic pregnancy: a double-blind randomized trial. *Arch Gynecol Obstet* 2015; 291: 939-943.
- van Mello NM, Mol F, Hajenius PJ, et al. Randomized comparison of health-related quality of life in women with ectopic pregnancy or pregnancy of unknown location treated with systemic methotrexate or expectant management. *Eur J Obstet Gynecol Reprod Biol* 2015; 192: 1-5.
- Sivalingam VN, Duncan WC, Kirk E, et al. Diagnosis and management of ectopic pregnancy. *J Fam Plann Reprod Health Care* 2011; 37: 231-240.
- Fernandez H, Campus P, Lucot JP, et al. Fertility after ectopic pregnancy: the DEMETER randomized trial. *Hum Reprod* 2013; 28: 1247-1253.
- Elson CJ, Salim R, Potdar N, et al. on behalf of the Royal College of Obstetricians and Gynaecologists. Diagnosis and management of ectopic pregnancy. *BJOG* 2016; 123: e15-e55.
- Barash JH, Buchanan EM, Hillson C. Diagnosis and management of ectopic pregnancy. *Am Fam Physician* 2014; 90: 34-40.
- Taejong S, Dong HL, Hwa ChK, Seok JS. Laparoscopic tube-preserving surgical procedures for ectopic tubal pregnancy. *Obstet Gynecol Sci* 2016; 59: 512-518.
- Mol F, van Mello NM, Strandell A, et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. *Lancet* 2014; 383: 1483-1489.
- Cohen A, Almog B, Lessing JB, et al. Laparoscopy versus laparotomy in the management of ectopic pregnancy with massive hemoperitoneum. *Int J Gynaecol Obstet* 2013; 123: 139-141.
- Hajibandeh S, Gumer AO, Wong CS. Laparoscopy versus laparotomy for the management of penetrating abdominal trauma: A systematic review and meta-analysis. *Int J Surg* 2016; 34: 127-136.
- Coste J, Job-Spira N, Fernandez H. Increased risk of ectopic pregnancy with maternal cigarette smoking. *Am J Public Health* 1991; 81: 199-201.
- Nio-Kobayashi J, Abidin HB, Brown JK, et al. Cigarette smoking alters sialylation in the Fallopian tube of women, with implications for the pathogenesis of ectopic pregnancy. *Mol Reprod Dev* 2016; 83: 1083-1091.
- Chouinard M, Mayrand MH, Ayoub A, et al. Ectopic pregnancy and outcomes of future intrauterine pregnancy. *Fertil Steril* 2019; 112: 112-119.