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RESEARCH ARTICLE

ECTOPIC PREGNANCY MANAGEMENT PLAN IN KING ABDULAZIZ UNIVERSITY HOSPITAL

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ABSTRACT

Introduction: Ectopic pregnancy is one of the most important complications due to its role in increasing maternal morbidity and mortality. Early diagnosis provides more chances to treat it without complications.
Aim: This study aimed to evaluate management plan of ectopic pregnancy
Method: This retrospective study screened the medical records of all women admitted to ER department at King abdulaziz University hospital as an ectopic case throughout 2012-2014.
Results: 120 patients were eligible and were included in this study. The mean age was 29.9±5.7 years. The mean of gravidity was 3.5±2.7. Thirty six (30%) cases had history of Pelvic Surgery and 21 (17.5%) had History of CS. All the 120 cases were admitted through emergency room (ER), 71 (60.7 %) had Vaginal Bleeding. Of the patients, 19 (15.8%) had expectant management, 42 (35%) received Methotrexate, 40 (33.3%) had laparoscopy & 18 (15%) had Laparotomy.
Conclusions: The treatment would be determined by the association of three main factors: clinical symptoms, ultrasound examination and β-hCG levels. Methotrexate is recommended for all womenwithout hemodynamic problems, unruptured pregnancyand low β-hCG. The earlier EP diagnosis the greater the chances of reducing maternal morbidity and mortality rate.

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INTRODUCTION

The first time to mention ectopic pregnancy (EP) was in the 11th century. It happens in 1-2% of pregnancies and presently it is defined as one of pregnancy complications and one of the major causes of maternal morbidity & sometimes mortality (Kopani *et al*., 2010; Skubisz *et al*., 2013). The prevalence of EP was increased during the last several years in all over the world, practically among group age 33-45 (Kopani *et al*., 2010; Parashi *et al*., 2014). Several risk factors need to be taken in concerns during diagnosis process, such as previous ectopic pregnancy, pelvic surgery, smoking, age (more than 40), history of abortion, previous genital infections, history of infertility and using reproductive technology, previous cesarean sections, and pregnant case with IUCD (Kopani *et al*., 2010; Parashi *et al*., 2014).). The clinical features of EP could be presented by abdominal pain, amenorrhea and/or vaginal bleeding.

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If any women presented with bleeding in early pregnancy it is important to exclude EP from the treating physician's diagnostic list (Kopani *et al*., 2010). Fallopian tube is the most common location of ectopic pregnancy (97%). The clinical manifestations of ectopic pregnancy made the diagnosis more challenging due to the wide broad spectrum of presentation between asymptomatic women until women coming with acute abdomen and even hemodynamic shock. The diagnosis of ectopic pregnancy depends on association between β-hCG levels and transvaginal ultrasound by 97 % sensitivity and specificity (Kirk *et al*., 2014; Refaat, 2015). The timely diagnosis of EP and the suitable treatment can reduce the maternal mortality rate. If the diagnosis was early with no ruptured EP and low BhCG levels in plasma the using of medical treatment (methotrexate) has been shown its safety and effectiveness (Kopani *et al*., 2010). Both treatment (medical or surgical) are effective, but the choosing of treatment plan depends on several factors such as ectopic pregnancy place, BHCG levels, and clinical scenarios (Kopani *et al*., 2010; Kirk *et al*., 2014; Refaat, 2015). This study aimed to evaluate management patterns of ectopic pregnancy among pregnant women admitted to the ER department at King Abdulaziz

University Hospital (KAUH), Jeddah, Saudi Arabia, between January 2012 and December 2014.

METHODOLOGY

Throughout 2012-2014, all patients admitted to ER department in King Abdulaziz University Hospital as an ectopic cases were included in this retrospective study. The medical records and registration books were retrieved to obtain the demographic (age, gravidity, parity) and medical information (β-hCG levels, ultrasound findings, medical or/and surgical treatment) with no direct contact with the patients. An ethical approval was obtained from the Biomedical Ethics Research Committee of King Abdul-Aziz University (KAU), Jeddah.

Statistical analysis

The data collected was analyzed using SPSS version 20 statistical software. Parametric data were expressed as mean and standard deviations (minimum and maximum) and non-parametric data were expressed as number (percentage). Chi – square test was used to find the relation between medical and surgical treatment. A P -value of <0.05 was considered significant.

RESULTS

During the period from January 2012—December 2014, 120 cases of EP were admitted to ER department, the mean age was 29.9±5.7 years while for gravidity & parity The mean scores were 3.5±2.7 &1.7±1.4) respectively. Fifty cases (41.7%) had normal BMI index, 25 (20.8%) had an underweight BMI index, 22 (18.3%) had overweight BMI index and 23 (19.2%) had obese BMI index. Concerning the risk factors & main complain, 10 (8.3%) had previous ectopic experience & 36 (30%) had history of pelvic surgery, 21 (17.5%) had previous cesarean secession, only 9 (7.5%) cases had history of Infertility. Seventy one cases (60.7%) were admitted with a main complain of vaginal bleeding, 109 (90.8%) were admitted mainly complaining of abdominal pain and from them, 79 (65.8%) had abdominal tenderness or rigidity. Thirty eight cases (31.7%) had cervical motion tenderness, 33 (27.5%) had adnexal tenderness and only 10 cases (8.3%) had an abdominal distension.

Table (1) BHCG levels

Variables	Mean ± SD	(Min-Max)
Level Of β-hCG at day 1 log	3.4±0.6	(1.9-4.9)
Level Of β-hCG at day 4 log	3.0±0.7	(0.8-4.2)
Level Of β-hCG at day 7 log	2.8±0.8	(0.9-4.3)
Level Of β-hCG at Follow up log	1.7±0.7	(0.8-2.9)

Data presented as Mean±SD

Concerning the investigation results, in 90(73%) cases the uterus was seen empty on ultrasound, 51 (42.5%) cases had adnexal mass measuring 2.9cm or less and 49 cases (40.9%) had a mass measuring 3 cm or more. Hundred and Ten cases (91.7%) had the tubal type of ectopic pregnancy 67 (55.8%) was in the right tube. BHCG was done for 95 cases (79.2%) in the first day with mean score of log (β-hCG level in day 1) 3.4±0.6 followed up with mean score of log (β-hCG level as follow up) 1.7±0.7 Table 1.

Regarding the treatment plan, 46 cases (37.0%) took Methotrexate, 40 cases took single dose, 5 took double doses and only 1 case took multiple doses. Forty cases (33.0%) had Laparoscopic surgery, 18 cases had partial salpingectomy and 16 had total salpingectomy. Only 18 women (15%) had a laparotomy surgery. A significant difference was demonstrated when comparing different treatment plans (medical and surgical treatment) (p<0.0001) Figure1.

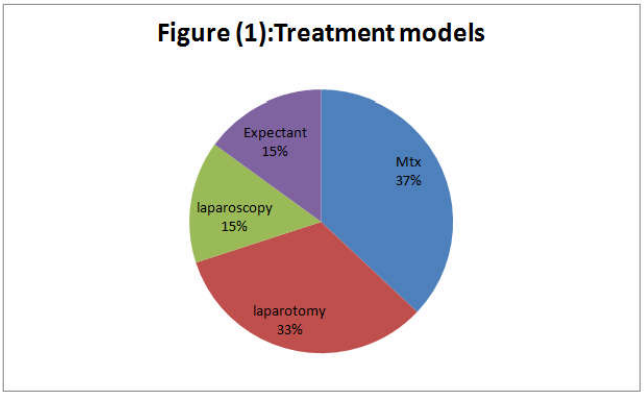

Figure (1) Treatment models

DISCUSSION

This study aimed to evaluate the management plan of ectopic pregnancy either if it was medical or surgical treatment and also to evaluate the factors which had influence on the success rates of different treatment. The first time to mention Methotrexate (Mtx) as a successful treatment for ectopic pregnancy was in 1980's by Tanaka *et al* since then several studies afterwards were conducted to determine the success rates which were ranging from 85% to 95%. In the study that was published on 2010 in Scandinavia, the successful rate was only 70.1%.Also, the study done in King Fahad Medical City in Riyadh, the success rate was 72 %. Two more other studies showed 100 % success rate including one in Makkah and the another one conducted by Nguyen *et al* on 2010. The results showed that from the 46 cases who received Mtx treatment, only 3 cases needed surgical interference which was addressed by an overall success rate of 90% and this is apparently within the international rates (Sendy *et al*., 2015; The Management of Tubal Pregnancy, 2010).

Comparison between single and multiple doses of Mtx was detected in several studies, some of the studies reported that multiple doses of Mtx are more effective than single dose and other studies stated that there is no difference in the efficacy between single and multiple doses of Mtx (Avcioğlu, 2014; Sendy *et al*., 2015). In this study, from the 46 cases received Mtx single dose,5 cases required double doses and one case required multiple doses, 3cases required surgical intervention due to ruptured EP or an onset of new severe abdominal pain. Methotrexate is a folic acid antagonist that targets rapidly dividing cells. In ectopic pregnancy, the drug stopped the generation of cytotrophoblast cells decreasing cell viability and β-hCG excretion and thus progesterone support for the pregnancy, which will help in dissolving the EP. The protocol of giving Mtx single dose is as the following:

Dose is calculated from the body surface area (50 mg/m2) using high& weight or using only body weight (1 mg/kg). This means that the majority of women will receive between 75 mg and 90 mg. Also the Serum βhCG levels provides a sensitive biomarker and should be used to monitor the response on Mtx treatment. It needs to be checked on days 4 & 7 from receiving the first dose of Mtx. If the βhCG levels have failed to decrease by more than 15% between day four and day seven, another dose must be given (Skubisz *et al*., 2013; The Management of Tubal Pregnancy, 2010; Sivalingam1 *et al*., 2011). On the other hand, the protocol for multiple doses consists of 4 doses in days 1,3,5 and 7 follows by leucovorine 'rescue-therapy' at a dose of 0.1 mg/kg on days 2,4,6 &8 (The Management of Tubal Pregnancy, 2010; Sivalingam1 *et al*., 2011; Lipscomb, 2007). McLaren *et al.* reported that the first time to mention the double dose of Mtx was in 2007 which had similar protocol to multiple doses of Mtx but it doesn't require extra citrovorum to avoid the side effects (Refaat, 2015; McLaren *et al*., 2014).

In this study only 3 cases among the 46 cases received Mtx needed a surgical intervention : 1 treated with Laparoscopy and 2 with Laparotomy due to several reasons, therefore gynecologists need to be careful when deciding to interfere surgically for patients who were under Mtx and had pain because this pain could be due to tubal abortion or stretching of the tube by a hematoma not to tubal ruptured (Avcioğlu, 2014; Dhar *et al*., 2011). Several factors influence the choose of surgical procedures, either laparotomy (LT) or laparoscopy (LS), LT was the traditional way and the preferred method if the patient had unstable haemodinamic levels, previous abdominal surgery or had body mass index more than 30, while LS became more accepted after the development of video laparoscopy and series of success of using LS in treating EP which were published in 1980s.

LS is the appropriate method in patients who had stable hemodynamic levels, women desire to save fertility. Also LS, reduce the morbidity, decrease the time for recovery after operation and the amount of analgesics drugs. In addition to all these factors, the skills of the surgeon performing the LS& the availability of equipment are very important and essential factors when choosing surgical models (Kopani, 2010; Refaat, 2015; Avcioğlu, 2014; Chaudhary *et al*., 2013). In the present study the patients who were treated with laparoscopy (LS) procedures were 40 (33.0%) and only 18 cases (15%) treated with laparotomy (LT) procedure. In this study, the rate of LS (33.0%) was more than LT (15%). While in the study conducted on 2010 in **"**Queen Geraldine" hospital, the LT rate was more than LS due to several factors (Kopani *et al*., 2010). Several studies stated that the common site of EP is the fallopian tube, in this study 92.5% of EP cases were tubal and 55.8% of them were in the right tube. Similar results were found in the study conducted by Agdi and Tulandi, 2008, they reported 93.1% of EP cases were tubal (Kopani *et al*., 2010; Agdi and Tulandi, 2009). For EP tubal pregnancy, Salpingectomy or Salpingostomy would be chosen depending on the clinical situation. If the patient suffered from bleeding, reccurent EP in the same tube or wide tubal damage, then Salpingectomy will be the preferred surgical procedure, while Salpingostomy will be the chosen one if the patient was stable haemodynamically, Ep less than 5cm, and practically preferred if the contralateral tube is absent or damaged (Refaat, 2015; Agdi and Tulandi, 2009; Mol *et al*., 2014). Expectant management is also one of the treatment models, it takes place when EP dissolve spontaneously through tubal abortion without any harm for patient. It is one of conservative strategies and can be used only under the following conditions: no evidence of ruptured EP, haemodinamicly stable woman, βhCG level is declining on regular basis, low level of progesterone hormone is detected. This kind of treatment needs constant follow up 3 times / week with β-hCG measurement and ultrasound imaging if necessary. βhCG levels under 1000 IU/l is a marker for success, several studies reported successful rate between 47%-82%. However, if βhCG level continued to be static or declining suboptimally, Medical or surgical treatments need to be considered. In this study only 19 cases (15%) were treated by Expectant management model (The Management of Tubal Pregnancy, 2004; Sivalingam1 *et al*., 2011). Ectopic pregnancy is a really dangerous problem with high morbidity and mortality rates especially if the diagnosis was late. The earlier the diagnosis was performed, the higher levels of successful treatment could be reached with less complications.

The association between serum βhCG levels and the ultrasonography measurements of the EP size are so important and necessary in assessing the rupture risks, determining treatment plans, and success rates estimations of conservative treatment. Several studies indicated that the Mtx had high rate of success when βhCG levels were <1500 IU/l and the diameter of the EP mass was smaller than 3 cm. while the use of surgical treatment is the first choice in the following situations: ruptured EP, unstable hemodynamic conditions, acute abdomen and hypovolemic shock or EP diameter more than 3cm (Avcioğlu, 2014; Sendy *et al*., 2015; Daniel *et al*., 2012). In the study conducted in Oman, the authors demonstrated that in order to reduce medical treatment failing rates, there is a need to follow accurate choosing standards in selecting patients who will receive Mtx (Dhar *et al*., 2011). On the other hand, the studies conducted in USA, France, New Zealand & KU recorded that Mtx treatment cost less than surgical intervention only if the βhCG levels lower than 1500 IU/l, no allergy of Mtx, and no ruptured EP which will reduce the failing rate and the need for surgical intervention (Sendy *et al*., 2015; Daniel *et al*., 2012).

Limitation

This study has some limitations, firstly it is a retrospective study which was depending on medical records and registration books, secondly all the cases were collected from only one medical health center and thirdly the limited number of cases (120) included in the study so further studies need to be conducted depending on multicenter aspect to cove more cases and to confirm the results.

Conclusion

The treatment will be determined by the association of three main factors: clinical symptoms, ultrasound examination and β-hCG levels. Mt X is recommended for all women without hemodinamic problems, unruptured EP and low levels of β-hCG.

It was demonstrated that the treatment by Mtx succeeded if the levels of β-hCG were reduced by 15 % in the 4th day of taking Mtx dose. The earlier EP diagnosis the greater the chances of reducing maternal morbidity & mortality rates. Even with good application of treatment protocols in KAUH, further studies need to be conducted and more improvement for management plansneed to be done.

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